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## SKELETAL CHANGES IN MALUM PERFORANS PEDIS

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The fact that osteomyelitis or a similar change in the bones is a factor of great importance as the underlying local pathologic process in perforating ulcer of the foot is insufficiently appreciated. This study is based on observations on 33 cases of malum perforans pedis. Perforating ulcer of the foot was first described by Vesigne in 1852, and the condition was designated by Leplat in 1855. The underlying changes in the bones are significant in explaining some of the basic factors of the condition. The skeletal changes in this condition were noted and described by Savoy and Butlin as early as 1879 in a paper which remains a classic. Bony sequestration formed a prominent feature of the clinical picture in then 5 cases. They stated that perforating ulcer might well begin in the depths of the foot or that the initial processes might begin almost simultaneously throughout the whole depth of the sole from the skin to the bone. This remarkable observation still forms the basis of any discussion of the pathogenesis of the disease today. Scaglietti in 1931 concluded that such pathologic change in the bones is secondary to the ulceration of the skin but is also in part independent of this, as is shown by the early primary trophic changes in the bone even when the cutaneous areas are not involved. He also expressed the opinion that the vascular changes are secondary to the cutaneous infection and are not primary, as the French believe. Finally, the changes in the bones must be considered coordinate with the cutaneous changes as there is no proof that the skeletal changes are the cause of malum perforans pedis.

A brief historical review revealed that all the known major etiologic factors in the disease, such as predisposition, familial tendency, trauma, arterial disease, disease and influences of the peripheral nerves and the central nervous system, pressure and constitutional diseases, such as diabetes and leprosy, were considered major factors between the years 1852 and 1873 and even earlier. The neuropathologic theory has steadily gained ground since then although there is still some difference

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of opinion as to the exact nature of the lesions. This theory is also supported by the fact that in even the mild varieties of leprosy, which has a remarkable affinity for the peripheral nerves, there are marked changes in the bones, and in many instances the nervous lesions predominate, although many of the changes are unquestionably due to bacterial invasion.

Defective innervation may favor the occurrence of ulceration in two ways: first, by leading to a break in the continuity of the surface, thus permitting the introduction of micro-organisms, and, second, by depressing nutritional activity and subsequently diminishing reactive resistance to the bacterial invasion. The skin and subcutaneous tissues are richly supplied with sensory nerves. Disordered nerve function may lead to profound changes in the tissues, for example, acute bed sores in a case of transverse myelitis within a few hours of the onset. Occasionally a lesion may appear or occur as a pure plantar lesion apart from any such influence as an incidence of trauma, suppurating wart or corn or even chronic epithelioma. All the etiologic factors may emerge as of primary or secondary significance in the pathogenesis. There is apparently a familial tendency, for the condition begins in many cases in early adolescence, as was indicated in our series by a study of the incidence according to age in decades. There were 2 cases in the first decade, 4 in the second, 3 in the third, 6 in the fourth, 8 in the fifth, 5 in the sixth, 4 in the seventh and 1 in the eighth.

It was evident from a study of our group that more than one factor was responsible for the disease, especially in case of such a basic disease as tabes dorsalis. This was illustrated in a man aged 45 whose foot was crushed sixteen years previously. Six years later there developed a typical ulcer. Subsequent periodic examinations revealed tabes dorsalis.

In this series the following etiologic factors were noted: diabetes in 6 cases, obesity in 1, vascular changes in 8, trauma in 4, encephalitis in 1, tabes dorsalis in 2, a familial tendency in 1, spina bifida occulta in 5, spina bifida manifesta in 1, traumatic myelitis in 1, a roentgen ray burn in 1 and frost-bite in 6. It is apparent that essentially there must be several basic factors, such as constitutional predisposition, trauma, constitutional diseases and vascular and nervous influences. Two main divisions would be sufficient for all clinical purposes: the idiopathic and the symptomatic. The term *malum perforans pedis* must therefore be interpreted as a generic term in order to clear up the present clinical confusion.

The variable known and unknown factors in the disease are readily appreciated from a brief consideration of the pathogenesis in some of the cases under consideration. In the 6 cases in which there was a history of freezing, ulcers formed on each foot five years later. Unilateral ulceration appeared fifty years after freezing in another case. In 1 other case of the same duration ulceration of both feet resulted. Of

57 cases of spina bifida manifesta entered in the records of the hospital we know of only 3 in which plantar ulceration resulted. Of course most of the patients were probably too young and had not yet subjected their feet to sufficient functional traumatization. Of 136 cases of spina bifida occulta with symptoms of sciatica, residual ulceration developed in only 1 and that only after the development of postdiphtheritic paralysis. It is generally conceded that weight-bearing and pressure effects are extremely important, as borne out by the fact that in some of the cases the ulcer healed while the patient was receiving treatment, which consisted chiefly of rest in bed, and as promptly reappeared after the beginning of weight-bearing.

This was strikingly exemplified in a man aged 59 years, who walked on the outer border of the foot following malunion of a compound fracture of the leg, with the formation of an ulcer on the outer border of the foot one year later. A study of the relative sites of ulcers also emphasized the significance of pressure effects.

The area of the joint of the big toe was involved in 14 cases, the region of the joint of the fifth toe in 12, the heel in 6, the lateral border of the foot in 3, the rest of the anterior portion of the arch in 10 and the dorsum of the foot in the 2 cases in which clawing was noted. In 7 cases lesions were present on both feet, in 3 there was more than one ulcer on the same foot. It is of interest to note the following associated anatomic abnormalities: hammer toe in 1 case, clubfoot in 4, clawfoot in 2, bunion in 1, spina bifida occulta in 5 and spina bifida manifesta in 1.

The condition predominates in men, chiefly because of occupations which necessitate added strain and traumatic hazards and probably because men are more liable to nervous and vascular disease, which seem to be important in the etiology of perforating ulcer. Of the 33 patients, 24 were males. The average age was 43 years, and the ages ranged from 13 to 77 years. The average age for the females was 34 years, and the ages ranged from 4 to 61 years.

Some authors have claimed that pain is contrary to the diagnosis of perforating ulcer. In this series there were 11 cases in which there was a definite history of pain (perhaps due to associated vascular disturbances), and in 10 the history was questionable. Of these there was moderate intermittent discomfort in 5. Of this group there were 2 cases of the idiopathic type and in the rest the condition was symptomatic. In the latter group there were 2 cases of diabetes, 2 of spina bifida, 2 with a history of freezing, 1 of tabes and 1 in which there was definite clinical evidence of vascular disturbance of the extremities. Pain as a symptom may therefore be present in degree and is dependent on the underlying general etiology and the extensiveness of the local pathologic changes. There is generally a localized area of anesthesia immediately surrounding the ulcer. There is usually very little tenderness on pressure, although walking may cause symptoms. The foot sooner or later



becomes the seat of other symptoms pointing toward impairment of the nerves or vessels such as increased growth of hair, hyperhidrosis (even bromidrosis), pigmentation and alteration of the nails

Adrian described the development of the ulcer as follows

- 1 A callus forms at one of the characteristic sites of predilection, with thinning of the epidermis and the formation of a blister. The contents are ordinarily serous but may be bloody after trauma. After this perforates or ruptures there is the usual formation of the ulcer.

- 2 The ulcer is obdurate and does not heal or may illustrate the characteristic tendency to periodic recurrent healing and reformation.

- 3 A residual deep ulcer forms, associated with tenderness and involvements of the bursae, bones and joints. Suppuration is now the rule, and the infection may burrow deeply and affect the tarsus even before it reaches the surface, because of the calloused soft structures. After partial destruction and elimination of bone occur, there follows shortening of the entire foot, as may occur strikingly in leprosy. Erysipelas, lymphangitis, abscess or cellulitis is frequently observed.

Scaglietti summarized the histologic changes as follows

- 1 In the skin there are an increase in the size of the sweat glands and hyperkeratosis. The base of the ulcer may have granulations, or the floor is covered or formed by dense connective tissue.

- 2 Changes in the bone occur chiefly in the metatarsophalangeal joints. Even when the joints are not involved by the cutaneous ulceration, the cartilage of the joints shows superficial necrosis. There are pannus-like formations and resorption of cartilage from the superficial and subchondral zone. If the joint is invaded, fibrous ankylosis or dorsal dislocation of the first phalanx is a minor consequence. The ends of the joint and part of the diaphysis may be destroyed. The ends of the diaphysis show concentric atrophy and pointed ends. In the metatarsal bones osteomyelitic changes usually follow infection of the joint, and all the following changes may be observed: necrosis of the suppurated portion of the bone, maximal porosis of the intact parts, formation of a subperiosteal abscess, periosteal osteophytes, sequestrums with granulation tissue and formation of a scar and, finally, healing after elimination of the sequestrums. The abscess cavity of the bone fills with new spongy bone, with inclusion of old dead bone in the new spongy trabeculae.

Scaglietti's studies also demonstrated the following histologic skeletal changes in three stages

- 1 Between the lacunar remaining parts of the old bone, new fibrous formations of bone, with islands of cartilage, appear in fibrous bone marrow.

- 2 Tiny new bone trabeculae become denser and more numerous and finally more and more mature until they are lamellar.

3 Bone becomes transformed and substituted by purely lamellar bone, in which trabeculae of small parts of the primitive bone and cartilage may be included as remnants of the first and second periods. The vessels show marked thickening of the intima, with narrowing of the lumen or thrombosis in different stages of organization.

The results of our studies bear out these observations and also emphasize the extensive collateral changes and tremendous regenerative efforts of the elements of the bones and joints, in spite of the intensive destruction present and the apparent hopelessness of the disease clinically. Our therapeutic experience and that reported in the literature was most discouraging so far as clearing up the local condition was concerned. Prior to their admission to the hospital 8 patients underwent some type of surgical procedure: drainage and sequestrectomy were performed in 2 instances, excision of the ulcer in 1 and amputation in 9 (7 of toes, and 2 of a foot). In the clinic, drainage was done in 12 cases, excision of the ulcer in 2, sequestrectomy in 3 and amputation in 12 (in 8 of toes and in 3 of a foot in toto, with amputation through the transmetatarsal joint in 1). Of this entire group healing occurred in only 2, and in 4 there was improvement.

It has been firmly established that an indirect method of attack directed toward improvement of the circulation must be utilized. Surgical procedures were developed and centered about the sympathetic nervous system following the observation of Claude Bernard in 1851. These procedures ranged from direct attack on the chains and ganglions of the central sympathetic system to the periaxillary decortication of Leriche. McClintic in 1929 recommended periarticular injection of alcohol instead, because the effect is immediate and less formidable. It is known today that effects obtained from a surgical procedure on the sympathetic nervous system are not permanent. All cases in which this type of treatment is to be used must be carefully selected after a thorough investigation as to the presence of vasospasm and vascular response following paralysis of the vasomotor fibers. Such dermatemic studies were made in several of our cases with little or no response, as attested by a definite rise in the surface temperature.

Because in so many cases of the disease there are primary or secondary vascular changes, it would appear that the pavaex method of vascular exercise is indicated either as a prophylactic or as a primary or adjuvant therapeutic measure. The amount of local surgical treatment is determined by the amount and degree of change in the soft tissue and bone changes in the bone being also largely secondary to ischemia. Although we have not had an opportunity to employ the pavaex method we strongly recommend its trial and make this suggestion in the hope that others will give it their favorable attention. It should do much to minimize the necessity for amputation.

## REPORT OF CASES

Because detailed histologic studies on amputated limbs affected by *malum perforans pedis* have not appeared in the English literature, the following analysis and study of a case is given

CASE 1 (figs 1 and 2)—*History and Course*—Ruth H., aged 8 years, was admitted to the hospital on August 1923. A varus deformity of the right foot had been noted since the age of 2 or 3 months, and progressive curvature of

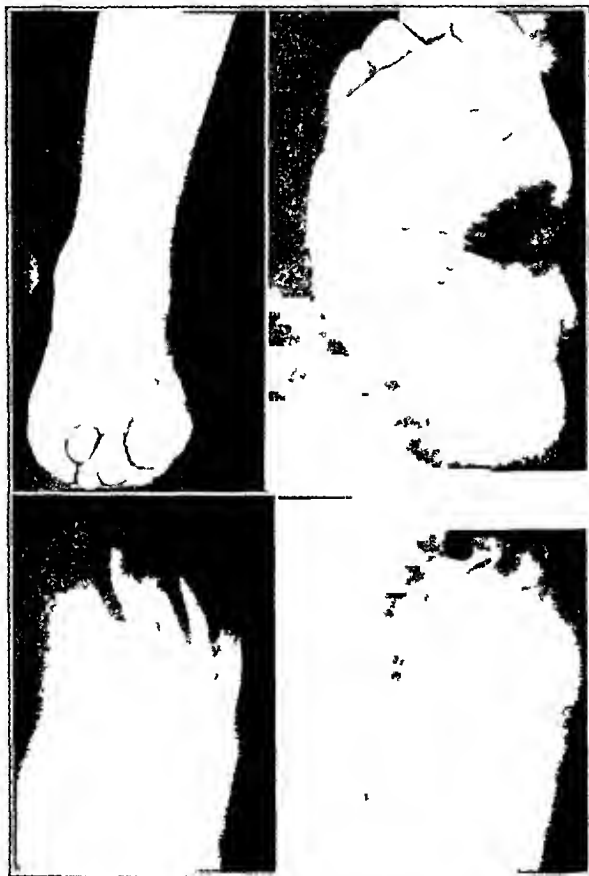


Fig 1 (Ruth H., case 1)—Photographs and roentgenograms of the condition diagnosed as chronic osteomyelitis with complete transformation of the bony structures, showing extensive destruction and characteristic osseous absorption

the spine had been present since the age of 2 or 3 years. The patient walked at 14 months. Examination revealed some trophic changes: the right foot shorter than the left by  $\frac{3}{4}$  inch (19 cm), slight varus, slight malformation of the nails and slight cyanosis. The flexor muscles of the toes and the peroneus muscles were weak, presumably a congenital weakness due to spinal malformation. The right knee jerk was sluggish.

An operation for spinal fusion was performed in 1926, followed by an uneventful recovery. Ulceration on the ball of the big toe appeared in 1928. It was

cleaned surgically and closed, but the wound never healed. The pathologic report stated that the diagnosis was chronic bursitis.

In 1933 there were three ulcers on the anterior part of the arch, with slight purulent drainage. In July drainage by the Orr method was instituted, and sequestrectomy of the first and fifth metatarsal bones was performed. There was considerable drainage one month later. In September a large area of devitalized skin appeared at the base of the big toe (fig 1). On September 15 the remainder of the fifth metatarsal bone was removed, and the wound was cleaned. The wound was closed tight, the cast was applied, and the wound healed. In October the wound had remained healed.

Laboratory examination gave negative results, and the dermathermic reading was unsatisfactory. Roentgenograms showed extensive destruction and charac-

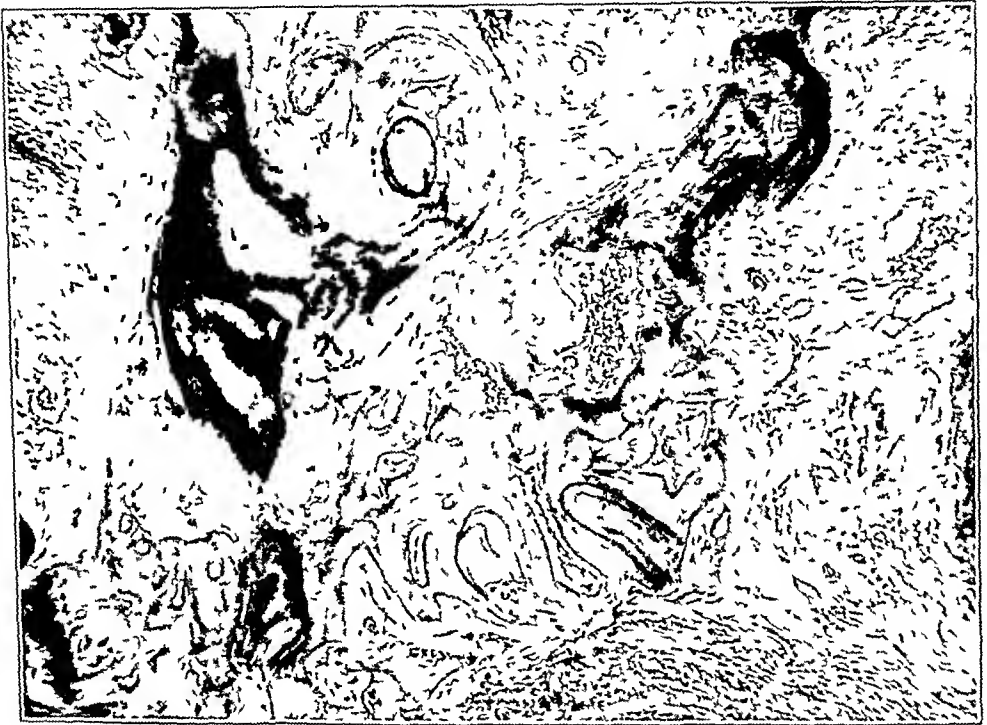


Fig 2 (Ruth H, case 1)—Photomicrograph of one section of the fifth metatarsal bone, showing radical pathologic changes.

teristic osseous absorption, chiefly in the metatarsophalangeal joints. The other bones were also extensively involved, and sequestration was present.

In 1934 amputation through the lower third of the leg was performed owing to the recurrence of ulceration and drainage. The stump healed.

*Examination of Metatarsal Bone*—The bone was very deformed. It was markedly thickened and somewhat shortened. The distal end was covered with joint cartilage which was thinned out and showed erosion in some places. The surface of the bone was irregular. The bone was cut longitudinally, and it was found to consist of rather dense spongy bone of normal hardness and of hyperemic fibrous bone marrow. There were no signs of suppuration or of necrosis.

Two slides were prepared for histologic examination. Both sections showed essentially the same picture (fig 2). There was a rather dense spongy bone with

very irregular structure. The bony trabeculae showed many blue cement lines, most of them typical lines of apposition, as signs of periodic apposition of bone. Some of the bony trabeculae were united by a rather young bone tissue of callous character, and the irregularity of the structure of the single bony trabeculae combined with callus formation between the bony trabeculae brought about the rather complex and irregular structure of the entire spongy bone. The bone marrow was fibrous, with many large capillary vessels. A considerable amount of chronic fibers of the fibrous bone marrow were separated from each other by edema and in other places by hyaline degeneration and by deposition of osteoid tissue. The cartilage of the joint was markedly thinned out by resorption from the cavity of the joint, with loss of the normal number of basophils but no necrosis of the cartilaginous cells. The peripheral portions of the cartilage showed complete resorption by a pannus-like formation from the synovial layers. There was not, however, a pannus-like formation of connective tissue on the surface of the cartilage itself. The synovia showed marked infiltration by lymphocytes and to a great extent by plasma cells. In one area close to the proximal end of the bone the marrow spaces were open, and the surface of the bone was covered with nonspecific granulation tissue. This granulation tissue blended with its deeper layers continuously into the fibrous bone marrow. The diagnosis was chronic osteomyelitis of the fifth metatarsal bone with complete transformation of the bony structure.

*Examination of Amputated Leg*—Dr Ernst Freund made the following analysis. The leg was amputated through the middle third, and formaldehyde was immediately injected into it. The foot was markedly deformed, especially by being shortened in the anterior half and by the dorsally subluxated contracted toes. The big toe overlapped the second owing to an extreme hallux valgus. The toe-nails showed signs of onychogryposis, with almost complete atrophy of the fourth and fifth toes. The skin on the dorsum of the foot exhibited hyperpigmentation. There was no thenar or hypothenar eminence on the plantar aspect, and the anterior portion was bulbous, densely calloused and scarred, but there was no evidence of ulceration. The joints and bones of the foot were inspected and prepared for histologic studies.

There were no gross changes in the tibio-astragaloid joint. However, marked degenerative arthritic changes were noted in Chopart's joint between the head of the astragalus and the scaphoid bone. The capsule was thickened and villous. The cartilage was degenerated unevenly and exhibited some marginal proliferative activity. The medial denuded area of the joint showed healing by a layer of fibrous tissue and cartilage. The anterior portion of the subastragaloid joint was similarly involved, while the posterior portion was unaffected, which leads one to conclude that no true communication exists between these portions and that this joint has no anatomic continuity. The anterior surface of the joint of the scaphoid bone did not show such marked changes as the posterior surface, but there was considerable atrophy of the cartilage, with peripheral retraction. The first metatarsal bone was destroyed in its anterior half, as was the adjoining portion of the first phalanx. The intervening joint was obliterated by a scar, which also filled a funnel-like depression fracture in this region. The second and third metatarsal bones showed destruction and were completely out of line with their respective phalanges. Dense scar tissue proceeded into these areas from the callus on the plantar surface. The fourth metatarsal bone, which exhibited in the roentgenogram (postamputation) typical pseudo-arthritis, revealed a well outlined cavity of the joint which was situated in the midportion of the bone. As the roentgeno-

gram showed very little of the fifth toe, this portion of the foot was prepared in toto for further microscopic examination. Portions of the entire foot were sectioned and stained.

**Astragaloscapoid Joint** The cartilage of the joint showed marked degenerative changes. Old hyaline cartilage was present, but in no place was there an entirely normal appearance. The surface was very irregular, the superficial layer with a horizontal direction of the cells had disappeared, and the ground substance was fibrillated. The superficial cell groups showed signs of proliferation. Large cell capsules formed and became gradually sequestered into the cavity of the joint. In other places, where the fibrillation of the surface of the joint was not so marked, the superficial layers of the cartilage showed partial disappearance of the hyaline ground substance, resembling fibrous more than hyaline cartilage. These changes extended far down into the pressure zone of the cartilage of the joint and were accompanied sometimes by the formation of fissures in a radial direction, with fibrinoid impregnation of the walls of the fissures. At the margins of the joints, especially at one side, typical exostoses had formed. The synovial tissue covered the thin cortex at the joint along a slightly lacunar line which frequently showed osteoclastic resorption. The zone of calcified cartilaginous tissue was at the central area of the surface of the joint and fairly well preserved. Toward the margins, however, the old zone of calcification had disappeared almost entirely. These superficial marrow spaces contained a hyperemic, loosely fibrous bone marrow. In many places osteoclasts could be seen busy with resorption of the bone and calcified cartilaginous tissue. The subchondral bone was slightly porotic and showed besides porosis, a pathologic structure. One was still able to outline easily the old thinned-out bony trabeculae running in a static way, chiefly radially, to the surface of the joint. Corresponding to the apex of the surface was a slightly osteosclerotic bony change, in the sense that between the old bony trabeculae irregular bony bridges of newly formed bony tissue appeared. This new bone was chiefly fibrous. It was also formed along the surface of the old bony trabeculae so that sometimes marrow spaces between bony trabeculae could be almost entirely filled out by new bone tissue. This picture resembled that of metastasis of osteoplastic carcinoma. It was of great interest, however, that the astragalus, which until now showed purely degenerative and not inflammatory changes of the cartilaginous and bony tissue, already showed this peculiar type of osteoporosis associated with a strong osteosclerotic factor.

**Anterior Subastragaloid Joint** The changes in the subastragaloid joint were essentially the same as those described for the head of the astragalus, though maybe a little more marked. Exostoses had developed at the margin of the joint but as yet did not surpass the level of the old surface. The subchondral bone tissue was porotic, but the osteoporosis was certainly on the way to repair. Most of the bony trabeculae were of complex structure. The central portion was represented by the old porotic bony trabeculae at the surface of which new bone had become apposed either in a straight line or more irregularly, sometimes forming bridges from one trabeculae to another. How these bridges form could be seen in one spot closer to the surface of the joint. Here were a few porotic old bony trabeculae embedded in loose fibrous bone marrow. Within the fibrous tissue and at the surface of the old bony trabeculae new spongy bone had formed irregularly, fibrous and in great part still osteoid. This formation of bone occurred primarily without the participation of osteoblasts. It was an infiltration process between the fibers of the fibrous bone marrow. One could follow all the stages of fibrous bone tissue from the first stage of infiltration with an edematous fluid to the more solid

stage of osteoid tissue, without sharp outline, and to the formation of bony trabeculae, with beginning calcification and surrounded by a dense layer of osteoblasts. All the changes could be considered as purely degenerative. There were no signs of inflammatory reaction. The invasion of the deeper cartilaginous layers from below in some places reached a pronounced degree. Marrow spaces had invaded the lower one half of the thickness of old cartilaginous tissue and had brought about a very irregular structure, with a mixture of old calcified and noncalcified cartilaginous, fibrous and fatty bone marrow, with osteoclasts and new bony trabeculae in the new marrow spaces. These pictures showed how the epiphysis gradually became enlarged by the recuperation of endochondral ossification at the cost of the old hyaline cartilaginous layer of the joint.

The changes at the posterior concave and anterior convex surfaces of the scaphoid bone were still typical of degenerative hypertrophic arthritis. The whole scaphoid bone showed more pronounced osteoporosis than that which could be observed in the astragalus and calcaneum. The subchondral bone tissue, however, showed the same kind of osteosclerosis, and all the stages from osteoid fibrous tissue to an almost complete obliteration of the marrow spaces by new bone tissue could be seen.

The skin of the big toe on the plantar side showed hyperkeratosis, which in some places was so marked that it could not be cut. But there were no defects in the skin caused by the formation of ulcer. It was surprising to note the great amount of sweat glands which with their hyperplastic convolutions of tubules occupied the subcutaneous fat tissue.

As far as the skeleton of the big toe was concerned, in no place could normal structures be found. The least amount of change was seen in the end phalanx. This showed considerable atrophy involving both the cortical and the spongy bone. Lacunar resorption was still going on at the outside of the cortex. The bony trabeculae of the spongy bone, although porotic, showed an abnormal amount of cement lines, which showed that the bone tissue had undergone, previous to the actual osteoporosis, changes with thickening by the apposition of bone. The bone marrow was almost pure fatty marrow, without any inflammatory signs. The joint between the proximal and the distal phalanx showed typical fibrous ankylosis, with slight subluxation of the distal phalanx. Old hyaline cartilage was present only as a very thin layer without any basophilic activity in the ground substance. The more superficial layers had disappeared by the process of incomplete cartilaginous resorption described by Weichselbaum and Pommer. The fibrous pannus-like formation on the surface was creeping over the cartilage of the joint. The cell groups, some of which were enlarged, formed the so-called lacunae. Under gradual disappearance of the ground substance between the cells, groups of the latter merged and became included in the fibrous tissue filling the joint space. The loss of hyaline cartilage of the joint was so marked in some places that the subchondral bony lamellae were denuded and at times even showed defects. It was interesting to observe that these defects sometimes again become repaired by a filling of a tissue which was at a stage between fibrous bone and calcified fibrous bone and calcified fibrous cartilage. So there were reparatory processes going on beside destructive changes. Altogether the pathologic picture was more quiescent. The proximal fragment of the big toe showed changes similar to those of the distal fragment as far as the bony structure was concerned. It was clearly shown that the present cortex derived its formation from a periosteal osteophyte of which the vertical arrangement of vessels was characteristic.

Whereas the distal end was more or less well preserved in its outline, the proximal end, which was supposed to articulate with the metatarsal bone, was destroyed to such a degree that there was nothing which would even suggest that once a joint was present. The bone ended rather abruptly with the diaphysis, with lacunar resorption at the outside of the cortex. The marrow cavity was open, and toward the proximal end the bone marrow showed more and more fibrosis, with hyperemia and some chronic lymphocytic infiltration, and blended gradually into an extensive area of scar tissue occupying the place where previously the metatarsophalangeal joint was present. There was almost nothing left of the metatarsal bone. An irregular piece of bone was included in the scarred soft tissue. The end of the joint could not be made out. The surface was still in an active phase of osteoclastic resorption. The bone was made up chiefly of lamellar bone tissue, quite sclerotic, and contained marrow spaces filled with fibrous bone marrow. The process appeared to be an attempt at regeneration of bone without gaining the real shape of a metatarsal bone.

**Second Toe.** The entaneous changes did not reveal any new features. Here again the number of sweat glands was surprising. The callus on the plantar side corresponding to the metatarsophalangeal joint was so extreme that the specimen had to be trimmed for purposes of cutting. The hyperkeratosis was marked. On gross inspection all the constituents of the toe were present. The metatarsal bone and first phalanx were considerably misshapen, but the second and third phalanges were markedly osteoporotic. The interphalangeal joint between the second and the third phalanx showed the cartilage to be well preserved. The changes caused by disuse of the joint in the first interphalangeal joint were more marked. The first and second phalanges formed with their long axis an angle of about 90 degrees, with slight plantar subluxation of the second phalanx on the first. Owing to this displacement the dorsal capsular structures were kept tight and exerted some pressure on the convex surface of the joint at the distal end of the first phalanx. This pressure combined with a lack of play in the joint brought about a pronounced thinning out of the cartilage of the joint in this special area. At the margin of the joint almost the entire noncalcified cartilage had disappeared. A cellular layer of fibrous tissue had formed, which included some polymorphonuclear cells (chondroclasts), busy with the resorption of the cartilage of the joint. The pressure, however, also had influence on the bony portion of the epiphysis in that area, where the intra-articular part was covered only by the periosteum and the synovial tissue. Here was marked osteoclastic resorption on the articular surface, with apposition of bone at the endosteal surface. This process of combined resorption and apposition led to a gradual deformity of the epiphysis, with flattening of that portion of the convex end of the joint which was out of contact with its antagonist and under pressure from the side of the tightened capsule.

Compared with the pronounced osteoporosis of the distal portion of the toe, the proximal part of the first phalanx and the entire metatarsal bone were in striking contrast, as they showed marked osteosclerosis. This osteosclerosis represented a healing stage in an inflammatory osteomyelitic process involving the proximal end of the first phalanx and the metatarsal bone. At the advanced stage of the process it is of course difficult to determine where the inflammation took its origin. It seemed, however, that the origin was in the metatarsophalangeal joint, and from there the adjacent bony portions were gradually involved.

The metatarsophalangeal joint was completely destroyed in its normal outlines and tissues. All that was present was an extensive area of scar tissue which extended from between the phalanx and the head of the metatarsus down to the



plantar surface of the toe. It was clear that this extension of scar tissue was a result of the healing of a sinus tract running down to an ulcer of the toe. But the scar tissue was by no means uniform or homogeneous. On the contrary, between the metatarsus and the phalanx, an irregular cleft with side branches was noted. The walls of the cleft formed by dense fibrous tissue tended to the formation of villi and even formed some synovial endothelium. This irregular cleft could be interpreted as a joint space formed secondarily in scar tissue, which fitted the place of the metatarsophalangeal joint after its destruction. It was a form of nearthrosis illustrating nature's attempt to maintain a joint in the metatarsophalangeal region. That this metatarsophalangeal joint was destroyed by a process quite different from that which led to the changes in the interphalangeal joints as described previously can be seen from the following observations:

1 The ends of the joint of the first phalanx and the metatarsal bone were entirely involved in a pathologic process. No normal hyaline cartilage was left. The cartilage covered the bone tissue irregularly and even extended continuously into the marrow spaces. This alone showed that there must have been a pronounced destructive process which led to the destruction of the ends of the joint. There was haphazard and incomplete regeneration of bone tissue. At the site of the metatarsus the regeneration was hyperplastic and abundant, whereas at the proximal end of the first phalanx it was deficient, leading to a diminution of the proximal end. The bone tissue found on each side was represented by spongy bone without static structure. It formed within fibrous bone marrow which was still hyperemic and showed here and there infiltration by chronic inflammatory cells. The bony trabeculae were in the stage of apposition. Thick layers of osteoblasts and osteoid bone could be seen almost everywhere, osteoclastic resorption inside the bones was relatively scarce, it was marked, however, at the surface of the periosteum. Toward the scar tissue occupying the place of the metatarsophalangeal joint the bone tissue dissolved gradually, the more isolated bony trabeculae. There were no continuous bony lamellae to separate the marrow spaces from the scar tissue.

2 The surrounding tissues, including scar tissue, frequently showed chronic inflammatory changes, with more diffuse or more circumscribed infiltration by lymphocytes and plasma cells.

3 There was one focus close to the metatarsal bone and, where included in scar tissue and surrounded by a form of fibrous tissue capsule, a small sequestrum could be seen lying in well preserved purulent exudate. This made us sure that this was the site of a formerly virulent suppurative process which at the time of observation appeared extinct. But to judge from this small focus of acute infection it would not have needed much stimulation for a flare-up.

As far as the bony structure of the metatarsal bone and the first phalanx was concerned, the typical picture of inflammatory osteosclerosis was present, as was well described by Scaglietti.

**Third Toe.** The cutaneous changes of the third toe were essentially the same as those of the other two toes. The first interphalangeal joint showed fibrous ankylosis, shrinkage of the capsule of the joint with obliteration of the peripheral portion of the cavity of the joint and thinning of the cartilage of the joint with subluxation by a pannus-like formation of fibrous tissue.

The metatarsophalangeal joint was gone, leaving no trace. Dense scar tissue occupied its former site, running down to the plantar surface of the skin, with hyperkeratosis. The scar tissue was rich in vessels and showed chronic cellular infiltration. In some areas it showed even older granulation tissue, with dense

infiltration by lymphocytes and plasma cells. A few muscle cells were included in the scar tissue with well preserved transverse striation. These changes showed that a short time previously in this area a more active suppurative process had been present which had quieted down.

Proximal to this area was an extensive massive formation of cartilaginous and bony tissue, which resembled in many respects the picture of osteochondroma or myositis ossificans. In this instance it probably represented extensive callus formation or, better, an attempt at regeneration of the metatarsal bone, which had been almost entirely destroyed. There was hyaline cartilage of a more embryonal type, in which the cells toward the periphery were more and more swollen (spherical), and the ground substance became calcified. Then from the surrounding fibrous tissue osteoclasts absorbed calcified cartilage and apposition of bone tissue took place at the surface of the calcified cartilage. Thus, spongy bone formed, which gradually became transformed into bone tissue of a more mature appearance. Calcification of cartilage and formation of bone tissue were so extensive that in the roentgenogram a dark shadow was cast.

The distal, small part of the metatarsal bone was present as a bony portion but no normal bony structure was seen. Fibrous bone marrow was densely infiltrated by chronic inflammatory cells. The bony trabeculae were of irregular structure, showing many blue cement lines, which frequently ran parallel to each other and to the surface of the trabeculae. The structure of the bony trabeculae became more complex the more one approached the area of the bony and cartilaginous callus formation. The marrow spaces showed dense infiltration, and among the infiltrated cells polymorphonuclears were by no means rare. The bony trabeculae were connected with each other by newly formed fibrous bone tissue, which was laid down in such an amount that the old bony trabeculae were covered from all sides with new bone tissue and the marrow spaces were almost entirely occluded. The old bony trabeculae were alive. This picture again resembled that of metastasis of osteoplastic carcinoma and in this instance it was due to sclerosing osteomyelitis. The osteosclerotic bone tissue surrounded an area interposed between the callus formation and the rest of the metatarsal bone. In this area many foci of puslike exudate were undergoing the process of organization. They became surrounded by loose fibrous tissue. In some places within the exudate small necrotic bony fragments were seen, sequestrums which either floated frequently in pus or became resorbed by polymorphonuclear leukocytes. Here again the picture was that of a subacute or even a chronic inflammatory lesion. Heretofore acute inflammatory signs had been minimal.

The proximal surface of the joint of the metatarsal bone was relatively well preserved. The hyaline cartilage of the joint was thinned out and became gradually resorbed from the margins, but there were no signs of necrosis and there was no more marked erosion of the cartilage.

**Fourth Toe.** The changes were essentially the same as those noted in the third toe, except that there was a disklike fibrous tab extending into the joint as an interposition from the shrunken capsule at the distal interphalangeal joint. The metatarsophalangeal joint was gone, and the area was supplanted by dense scar tissue. There was a fracture of the shaft of the metatarsal bone, with no signs of healing.

**Fifth Toe.** The most marked changes were seen in the metatarsal bone, in the joint and in the proximal end of the proximal phalanx. The shaft was almost entirely gone, and the degenerative changes predominated, with no signs of acute inflammation.

Brief reports of five other cases are included

CASE 2 (fig 3)—Edith S, 4 years of age, was admitted to the hospital in May 1922 with a diagnosis of spina bifida, congenital calcaneovalgus, perforating ulcer and osteomyelitis of the os calcis

The child was under observation over a period of eight years. Her case illustrates the effects of pressure due to the deformity of the calcaneum on the basis of a myelodysplasia of the spinal cord, as evidenced by the complete cleft between the sacrum and the first lumbar vertebra. Ulceration followed blistering and

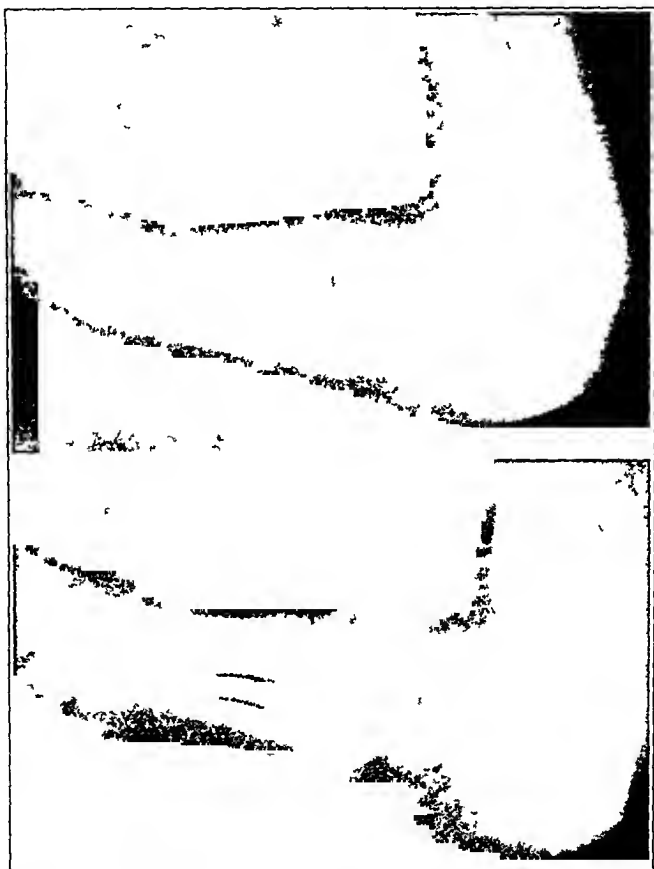


Fig 3 (Edith S, case 2)—Roentgenograms showing the effects of pressure caused by deformity of the calcaneum, attributed to myelodysplasia of the spinal cord

persisted intermittently over the entire period of observation. In 1924 the os calcis was operated on by the split heel approach according to the Orr method. The wound healed, although necrotic bone was encountered at operation. Sensation was always intact. Ulceration recurred later.

Examination of one section revealed chronic osteomyelitis with inflammatory osteosclerosis, with a tendency toward healing. The section of skin was remarkable for the formation of an epithelial cyst undoubtedly of traumatic origin. Owing to the ulceration of the skin, displacement of epithelium into the deeper portion of the subcutaneous tissue accounted for the formation of a cyst.

CASE 3 (fig 4) —Albert P., aged 53, was admitted to the hospital in October 1933. He had bruised his foot on a cinder six months previously, while wearing thin-soled shoes. An open sore soon developed, which healed and reopened. At the time of admission to the hospital there was drainage of three months' duration. Three years previously the patient had experienced lancinating pains in the legs.

Examination revealed an ulcer on the ball of the foot, with foul discharge. The entire foot was swollen, discolored, cold and clammy. The roentgenograms strongly suggested the changes that occur in cases of leprosy. The metatarso-

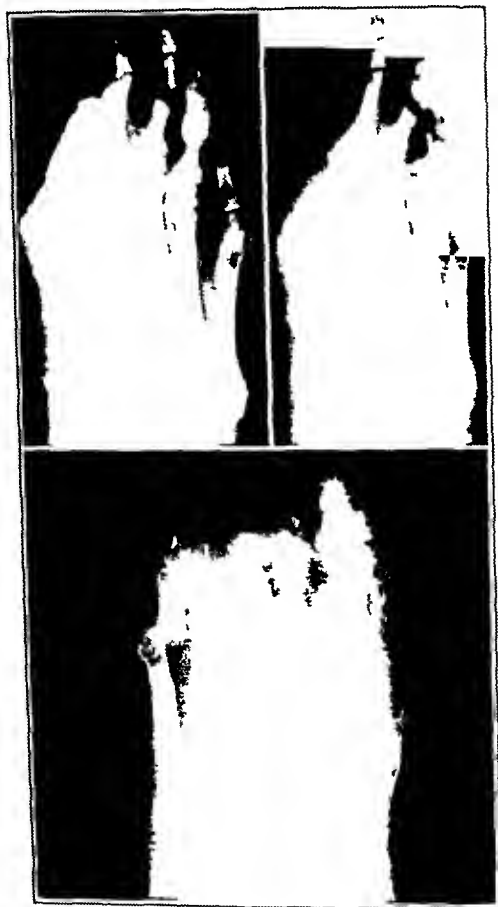


Fig 4—The upper roentgenograms show compound fracture of the first metatarsal bone, necessitating resection. This type of direct infection does not produce the general changes noted in cases of perforating ulcer. Compare them with the lower roentgenogram (Albert P.), in which the changes suggest those that occur in leprosy. The metatarsophalangeal joints and their contiguous bony elements are typically destroyed and are undergoing resorption.

phalangeal joints and their contiguous bony elements were typically destroyed and were undergoing resorption. The reaction to the Wassermann test was negative. The sugar content of the blood was 297 mg per hundred cubic centimeters. A diabetic regimen was indicated. Permission for amputation was refused.

Case 4 (fig 6)—Fred N, aged 33, was admitted to the hospital in August 1933. The patient had always had difficulty with his feet but did not have real pain at any time. Six months previously an ulcer appeared at the end of the second toe on the right foot, which healed after a piece of dead bone was removed. The third toe was similarly affected one month after this, and at the same time a blister developed on the second toe of the left foot. The patient opened the blister, and an ulcer developed, which persisted. There was no history of trauma or freezing. The patient walked fairly well.

Examination revealed an ulcer the size of a dime on the ball of the big toe of the left foot which was sharply demarcated but rather ragged. Part of the nail was missing on the big toe of the right foot, and the entire toe was short. The third toe of the right foot was thicker than that of the left foot and had a



Fig 5—Recurrent perforating ulcers of the toes and heels in a young woman subsequent to an attack of epidemic encephalitis and associated with osteomyelitis of the phalanges. These episodes were all due to combined nervous and peripheral vascular disturbances which were uninfluenced by lumbar ramisection performed bilaterally about eight years before the photograph was taken. In the photograph the ulcers have healed, as they always did following a period of rest and relief from weight bearing.

small ulcer at the distal end. The ulcers were painless. The neurologic examination gave negative results.

Roentgenograms showed spina bifida occulta of the first sacral segment. The anteroposterior views of the feet revealed marked hallux valgus of the right foot, with some subluxation of the proximal phalanx. There was a defect of the third phalanx of the second toe, with no intrinsic pathologic process of the right foot.

The first phalanx showed increased width. There were some irregular periosteal thickening and proliferation, with the formation of small exostoses. There was no definite swelling of the soft tissue of the big toe of the left foot.

Dermatometric readings after injection into the posterior tibial nerve showed the basic temperature on the right side to be 29.6 C and after thirty minutes 30.9 C, and on the left side, 29.9 C, and after thirty minutes 29 C.

Treatment started on September 1 included resection of the ulcer of the big toe and plastic closure, with some improvement. On October 25 a Mayo amputation was performed on the left foot. The wound healed. A pathologic examination of soft tissue removed at operation revealed a torpid cutaneous ulcer with hyperplasia of the sweat glands and slow and irregular epithelization from the margins. The diagnosis was early perforating ulcer of the foot caused by circulatory insufficiency, with few changes in the bone.

CASE 5 (fig 7)—Isabell M., aged 6 years, was admitted to the hospital in March 1927. The child was born with a meningocle over the lumbar region and a club foot (left). The meningocle was surgically removed. The roentgenogram showed a complete lumbar and sacral cleft. In 1927 a small ulcer



Fig 6 (Fred N., case 4)—The anteroposterior views of the feet revealed marked hallux valgus of the right foot, with some subluxation of the proximal phalanx. There was a defect of the third phalanx of the second toe, with no intrinsic pathologic process of the right foot. There was no evidence of abnormality of the spine.

developed on the lateral surface of the ball of the foot, which was painless and healed slowly. In 1929 the foot was more markedly deformed, and the ulcer again appeared and persisted. This was on the lateral weight-bearing surface. Surgical correction and stabilization of the foot was performed. The operative wound healed, but the ulcer had not after some months. Two years later all signs of ulceration had disappeared, and the fusion of the foot held firmly. In 1932 an ulcer developed on the big toe of the same foot, with some moderate drainage. This continued until osteomyelitis set in in the proximal phalanx. Operation was performed according to the Orr method. The bone was friable, fragmented and sequestered, and there were considerable reddish granulations but no free pus. The wound healed in about eight months. Staphylococcus was recovered from the wound at the time of operation.

Histologically the bone showed lacunar absorption, and the tissue between the trabeculae was filled with granulation tissue densely infiltrated by inflammatory

cells, of which the polymorphonuclears predominated. The diagnosis was chronic osteomyelitis, with a perforating ulcer of the foot.

CASE 6 (fig 8)—Earl T, aged 33, was admitted to the hospital in March 1933. Ulceration followed local injury to the foot three years previously. There were some pain, heat and redness over the bunion area for several days before drainage set in at the outset of the formation of the ulcer. The area healed with rest after two weeks. In October 1932 there was a recurrence, with a plantar lesion over the same area. During the same winter the opposite foot became similarly involved. Some swelling of the ankles persisted with prolonged weight bearing, because the patient did not stop working. Both feet had been frozen five years previously.

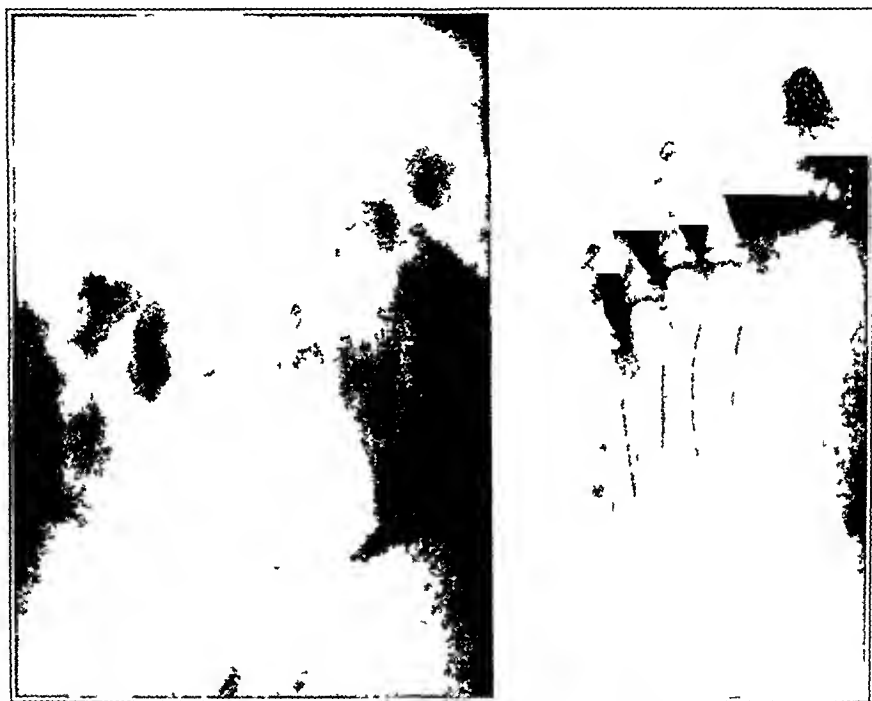


Fig 7 (Isabell M, case 5)—The roentgenogram of the spine shows a complete lumbar and sacral cleft. The other roentgenogram is of the club foot (left).

The family history revealed that the mother suffered from callosities. A maternal aunt was similarly affected, and her daughter had a painful condition of the foot which recently required the removal of a small piece of bone.

Examination revealed the right foot and leg to be edematous, and the fore part of the foot was especially red on the dorsum. There was pitting edema, but the foot was not tender. Under the large toe was an ulcer  $\frac{3}{4}$  inch (1.9 cm), with considerable oozing. Two smaller toes had dark shiny calluses which looked like areas of beginning dry gangrene. There was a marked hallux valgus on the left foot, the nails were hypertrophied, and the sole had two calluses, in one of which was an ulcer. The reflexes were slightly hyperactive.

The laboratory examination gave negative results.

The dermathermic reading after thirty minutes showed an increase of 0.8 C. Before injection the temperature was 28.7 C. The anteroposterior roentgenogram of the feet showed an enormous widening of the anterior portion of the arches. The first metatarsal bone of each foot was in a position of marked adduction. There were destructive lesions at the distal end of the fifth metatarsal bone of the left foot, on the distal two thirds of the first phalanx of the big toe of the right foot and on the head of the metatarsal bone of the second toe of the right

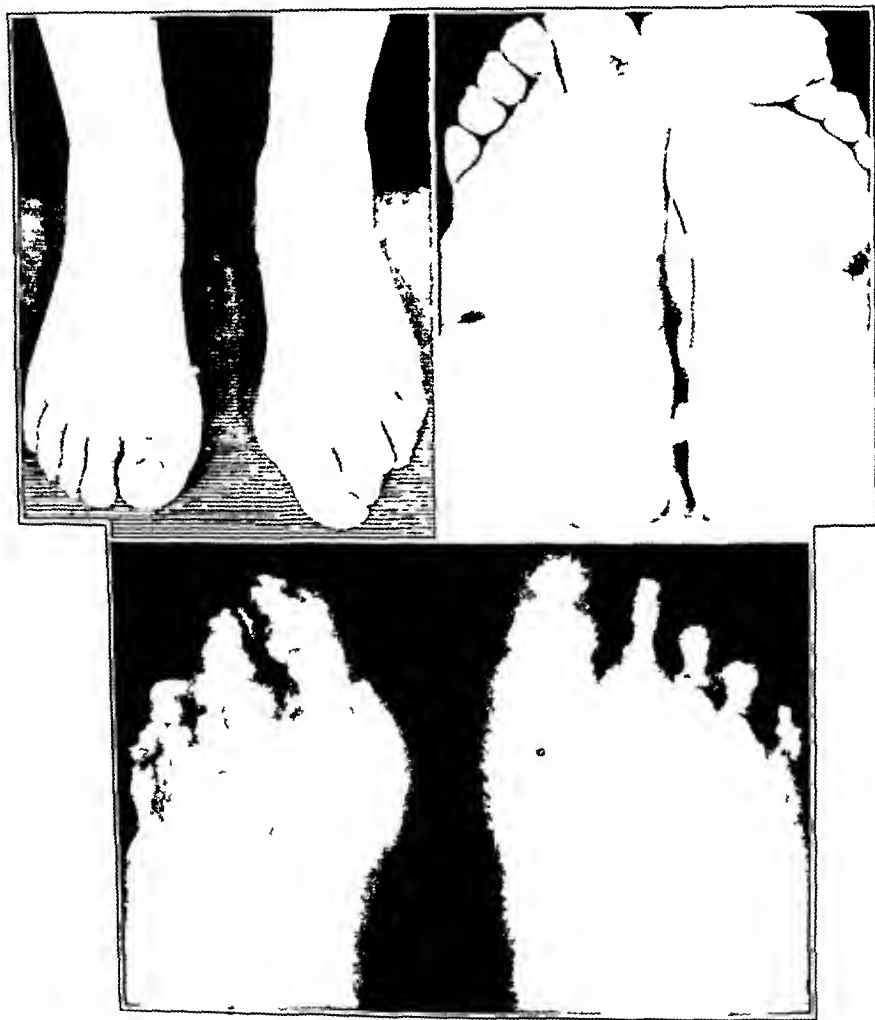


Fig 8 (Earl T, case 6)—Photographs and roentgenogram showing involvement of both feet following local trauma to one foot three years previously

foot. There were destructive lesions of the second interphalangeal joint of the big toe of the right foot and of the fifth toe and of the metatarsophalangeal joint of the fifth toe of the left foot. There were peculiar destructive processes at the distal end of the end phalanx of each toe of the left foot. Periosteal reaction was present along the diaphysis of the third and fifth metatarsal bones of the left foot, and of the first, second and third metatarsal bones and along the first phalanges of the first and the second toe of the right foot. There was marked swelling of



the soft tissue of the big toe of the right foot, the roentgenogram showed activity in the first and second phalanges, whereas all the other lesions seemed to be of longer duration and in a more chronic stage. The distal end of the fifth metatarsal bone of the left foot was completely destroyed, and there was subluxation of the toe in a dorsal direction. The lesion was that of an osteomyelitic process of the metatarsal bone and of the phalanges, including the joints. A specimen was removed for biopsy, consisting of the proximal phalanx of the big toe and the heads of the metacarpal bones. There were edema and thickening of the tissues. The periosteum was thickened and adherent. Concentric lamellations were noted on removing the cortex. The bone was hemorrhagic, and a definite medullary cavity was not noted. The wounds healed in four days by first intention. On May 18 treatment was instituted with a whirlpool bath and irradiation with ultraviolet rays, with considerable improvement. Examination on October 6 revealed the ulcers to be healed, but in July that on the big toe of the right foot reopened, and one week later that on the left foot reappeared. These were present with some swelling at the time of writing.

A piece of skin and three small pieces of bone taken from the first metatarsal bone were examined histologically. The piece of skin showed marked thickening of the subcutaneous layer, which was entirely composed of fibrous tissue. The subcutaneous fat tissue had completely disappeared. Chronic cellular inflammation was present in some places but did not form an outstanding feature. The pieces of bone taken from the first metatarsal bone showed irregular but dense spongy bone. The bony trabeculae were composed of fibrous and lamellar bone of almost equal amount. They were included in dense and hyperemic fibrous marrow. The bone tissue seemed in a quiescent stage. There was not much resorption or apposition of bone. The new bone was almost entirely the result of formation of fibrous bone originating in the fibrous bone marrow. There were no signs of acute inflammation.

Several small pieces of bone taken from the second metatarsal bone showed essentially the same picture as that of the first metatarsal bone. Fibrous bone marrow was present, with many hyperemic vessels. The spongy bone was even more irregular than that in the first metatarsal bone, especially was lacunar resorption in the marginal portions of the metatarsal bone very mixed.

The diagnosis was chronic osteomyelitis of the first and second metatarsal bones without signs of a specific pathologic process.

#### SUMMARY

We have discussed the general features and the changes in the bones in cases of *malum perforans pedis* as based on observations on a series of 33 cases. It is evident that any treatment to be effective must be aggressive and must be instituted almost early enough to be considered as a prophylactic measure. Therapeutic methods must aim at rectifying any or all underlying constitutional causes that are operative, as well as the local condition. It is safe to assume that any improvement in the circulatory status of the affected member will react favorably on such skeletal changes as are more or less collateral and which consist chiefly of degenerative changes due to atrophy of disuse and local pressure at the joints. There is a marked tendency to repair and regeneration. It is suggested that the pavaex treatment offers an excellent means of

obtaining an improvement in the local circulation. Those areas which are definitely osteomyelitic must be considered as involved in primary direct inflammatory changes superimposed on the basic degenerative transformations and are due to infection directly by way of the break in the surface of the skin. This is supported by the fact that in a series of over 130 cases of osteomyelitis of the small bones of the foot the condition in the vast majority was due to a perforating injury. In the series of over 1,500 cases of osteomyelitis there were only 8 instances of peripheral metastases to the bones of the foot. Therefore we believe that all osteomyelitic foci in perforating ulcer of the foot should be radically attacked as in any other osteomyelitic localization. There must be a careful clinical evaluation of the bony changes as seen in roentgenograms in order to distinguish the osteomyelitic from the collateral changes. The presence of sequestrums is of great aid in forming an accurate opinion and indication. Amputation should be resorted to only after all else has failed and with the thought that ulceration has been known to recur in the stump and also in the other foot after it has taken up its added static burden.

# RÔLE OF THE ILEOCECAL SPHINCTER IN CASES OF OBSTRUCTION OF THE LARGE BOWEL

LOUIS SPERLING, M D

MINNEAPOLIS

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It has been known for a long time that distention of the small bowel is rarely observed in cases of obstruction of the colon. The older German writers, Kieuter, Anschutz and others, have explained this observation by assuming that the ileocecal sphincter is competent to withstand back pressure. The literature from 1890-1900 is replete with reports of cases of obstruction of the colon in which gangrene and perforation eventually developed with absence of distention of the small bowel. The more recent literature on obstruction (Buiget and Gatch and their associates and others) has stressed the fact that changes in the wall of the bowel are more likely to occur in cases of obstruction with a closed loop than in those of simple type.

The importance of the ileocecal sphincter in obstruction of the large bowel depends entirely on whether it is competent to prevent backflow into the ileum, thus converting an otherwise simple type of obstruction into a closed loop.

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From the Department of Surgery of the University of Minnesota

Submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science (September 1934)

This thesis deals with the question of why obstruction of the large bowel, especially that due to carcinoma of the left half of the colon, is of a closed loop type and whether the ileocecal sphincter is sufficiently competent to prevent regurgitation of gas and fluid into the small bowel until the increase of intra-enteric pressure is great enough to compromise the circulation of the wall of the large intestine

The work is divided into four parts

1 Experimental study of the competency of the ileocecal sphincter in cadavers, dogs and clinical subjects

2 Observations on the intra-enteric pressure which may obtain in clinical cases of obstruction of the large bowel

3 Experimental study to determine the effect of such recorded pressures on the structure of the wall of the bowel

4 Presentation of clinical cases

The value of this work is twofold. First, it emphasizes that obstruction of the large bowel should be treated as a closed loop or a potential strangulating type. Second, for the first time measurements of the increased pressure which obtains in cases of obstruction of the large bowel are recorded.

#### REVIEW OF LITERATURE

An enormous literature has accumulated concerning the pathologic physiology of intestinal obstruction, but it has dealt mostly with the variety seen in the small bowel. Relatively little attention has been paid to obstruction of the colon, and a tendency to regard it in the light of recent observations on ileus of the small bowel is evident. The difference between ileus of the small bowel and that of the large is chiefly one between simple obstruction and that of the closed loop type, and it depends on the presence of a competent ileocecal sphincter, which prevents backflow and allows intra-intestinal pressure to mount to dangerous heights.

Bauhin described the ileocecal sphincter in 1605 and conjectured that it was competent to resist back pressure, acting chiefly in the mechanical rôle. This was accepted for about three hundred years without question. However, in the last fifty years much has been said and written with reference to the competency of the ileocecal sphincter to withstand the injection of fluids or the insufflation of gases into the rectum.

That the valve acts not only mechanically but as a true sphincter was emphasized by Cannon and also by Rutherford who demonstrated the presence of circular fibers. Balh through important histologic studies not only confirmed the work of Rutherford but demonstrated the presence of oblique fibers. The valve acts then as a real sphincter, similar

to that of the pylorus, and regulates the passage of chyme from the small bowel into the large and effectually prevents regurgitation

Elliot has shown that the ileocecal sphincter is not an essential organ, i. e., it is absent in the bear, ferret and hedgehog. It is not essential to life, as patients on whom resection of the ileocecal region and ileocolostomy have been performed apparently accommodate themselves to the change after a short period of diarrhea and experience no further trouble

#### ANATOMIC STRUCTURE OF THE ILEOCECAL SPHINCTER

In textbooks of anatomy (Sobotta and McMurrich) the ileocecal sphincter is described as formed by two folds of mucous membrane, which are termed the upper and lower lips of the valve. The deeper layers of the lips are the two muscular layers of the ileum. The fold appears as a hemispherical papilla 1.8 cm. in diameter projecting 1 cm. above the cecal wall. The surfaces of the lips directed toward the large intestine have the character of the mucous membrane of that portion of the intestine, while those that are turned toward the lumen of the ileum are covered with villi to the edges of the valvular orifice. When open the lips of the valve are separated by an elongated slit pointed at either end, and when in contact they form a complete closure between the large and the small intestine. From the lips of the valve semicircular folds radiate to the anterior and posterior portions of the wall of the cecum. They are termed the frena (anterior and posterior) of the valve, and they form the boundary between the cecum and the ascending colon.

#### NERVE SUPPLY

Elliot has demonstrated that the motor innervation of the sphincter is through the ninth to the twelfth thoracic nerve and the first and second lumbar segments of the splanchnic nerves. He obtained contraction by stimulation of these nerves and by painting the sphincter with epinephrine. Elliot's observations were confirmed by Hiomada and by Dale. Stimulation of the vagi and the pelvic nerves did not result in contraction. Walcker cut the ileocolic nerves, and paralysis of the sphincter resulted. The sphincter becomes incompetent after section of the spinal cord (Elliot). Tonnies cut the postganglionic fibers to the ileocolic and midcolic arteries and the rami communicantes of the twelfth and thirteenth nerves on each side and noted paralysis of the sphincter. There was also paralysis if the splanchnic nerves were cut in the chest. Hinrichsen and Ivy studied the innervation of the ileocecal sphincter and came to the following conclusions:

- 1 The sphincter acts physiologically
- 2 Stimulation of the vagus produced first relaxation, followed by a strong contraction, therefore, the vagus has both motor and inhibitory fibers

3 Stimulation of the splanchnic nerves resulted in contraction only, i. e., the splanchnic nerves maintain the tone of the sphincter.

4 Contraction may occur following stimulation of almost any abdominal nerve and from distention of the stomach, duodenum or colon.

5 Contraction during the feeding reflex is due to a duodenocolic reflex.

The effect of the duodenocolic or the gastriocolic reflex on the sphincter has been mentioned by several writers. Hannes found that the ileocecal sphincter is open in dogs except after the intake of food. Tonnis showed that when the stomach is full the sphincter remains closed and that it opens only with the onset of peristalsis in the ileum. Examination one hour after a meal seldom showed the presence of incompetency. From this it would appear that filling of the ileum by a barium enema is no index of insufficiency if the enema is taken on an empty stomach during fasting or long after a meal. That the nerve control of the sphincter is chiefly through the local portion of the intramural plexus of Auerbach was shown by Short, who observed in experimentation on a man with the ileocecal sphincter exposed through a cecostomy opening that stimulation of the folds of the cecal mucous membrane when it was in full activity after a meal delayed outflow from the ileum and made the jets less frequent, though it did not stop them altogether. It is conceivable that the irritation set up by distention of the cecum and stasis of fluids and gases due to stricture of the left portion of the colon would result in increased tone of the sphincter, making it more competent in a person with obstruction than in a normal person.

From the experiments of Heile it seems that filling of the colon causes a firmer contraction of the sphincter, for in experiments performed for a different purpose he showed that the introduction of a tampon cannula into the colon produced a much slower evacuation of the small bowel through the appendical fistula. This may be due to increased contraction of the muscle fibers of the sphincter after mechanical irritation produced by gradual filling of the colon. Sudden massive filling of the colon, such as occurs with the barium enema, is not to be compared with the gradual distention in cases of obstruction of the large bowel.

Case stated that reversed waves are the prevailing type of movement in the proximal portion of the colon and that they may become exaggerated in the presence of obstruction of the left half of the bowel resulting in stasis in the proximal segment. He called attention to the fact that many writers have described instances of gangrene of the cecum associated with obstruction of the pelvic portion of the colon, and he explained the phenomenon as due to waves of antiperistalsis originating at a ring of tonic contraction, which create back pressure and result in

distention of the cecum Blamoutier definitely observed this ring of contraction from which waves of antiperistalsis seemed to originate He commented on the fact that the ileocecal sphincter would soon atrophy if it were not for the presence of these reversed waves

#### COMPETENCY OF THE SPHINCTER

In 1586 Piccolhomini showed that injection of air or water through the rectum produced closure of the ileocecal sphincter Fabricius ab Aquapendente (1618) was unsuccessful in injecting air through the rectum into the ileum Postmortem tests of incompetency of the sphincter have been made by many investigators Rutherford summed up the results of these tests as follows "Want of uniformity in description makes it probable that the ileo-cecal valve changes soon after death" He concluded that normally the valve is competent during life The fact that the ileocecal valve acts as a muscular sphincter makes it evident that its competency must depend on the tonicity of its muscle fibers and that all factors influencing the tone of the ileocecal region, whether of local or of remote origin, also regulate the sphincter

On the assumption that the valves act mechanically only, Plesch compared them to a pair of lips and indicated that there would be no incompetency when the lips were accurately apposed to each other

The degree of increased colonic pressure required to force the ileocecal sphincter has been investigated by many workers Cannon noted that in a cat large enemas were passed into the small bowel but that small enemas were not Von Genersich forced from 6 to 9 liters of water into the colon under a pressure of from 80 to 100 cm of water and found that the fluid passed into the small bowel He observed this in both living and dead subjects This was confirmed by Dauriac Von Ziemssen forced carbon dioxide into the colon in both man and the dog In dogs he was able to recover it from the mouth, in human subjects he recovered it only when a high pressure was used Senn found that air under a pressure of 2.5 pounds (1.1 Kg) per square inch (6.45 sq cm) could be passed from the anus to the mouth in man However, the ileocecal sphincter withstood a pressure of 0.7 Kg successfully, and only when the pressures exceeded 0.9 Kg was colo-ileal regurgitation evident In his experiments on dogs he concluded that the ileocecal sphincter resisted a pressure of from  $\frac{1}{2}$  to  $\frac{3}{4}$  pound (0.2 to 0.3 Kg) In experiments in which fluid was forced through the ileocecal valve, multiple lacerations of the peritoneal surface of the large bowel were shown at autopsy Walcker inflated the cecum in cadavers and found that the sphincter withstood a pressure of from 2 to 80 mm of mercury In 1 specimen the valve withstood the increase of pressure until the cecum ruptured Burt determined by the introduction of air

the pressure required at various levels to rupture the bowel. He found that the cecum had the least resistance, rupturing at a pressure of 1.53 pounds (0.69 Kg) per square inch (6.45 sq cm). Joltian, Baufle and Coope (cited by Larson and Borgen) produced pressures of various degrees in the large bowel and noted the effects. They found that the normal colon could hold about 1,000 cc of fluid, which they computed was under a pressure of from 16 to 20 cm of water. When the pressure was increased to about 30 cm of water with a volume of 3,000 cc in the colon the patient complained of pain and distress.

Heile stated that a pressure of 20 mm of mercury is the highest that will be withstood by the ileocecal sphincter although in some cases he observed rupture into the peritoneal cavity.

The percentage of cases of insufficiency of the ileocecal sphincter as reported by various roentgenologists varies from 0 to 90 per cent. Groedel has never seen incompetence of the valve in withstanding contrast mediums in healthy persons. Drummond and Schwartz noted that enemas rarely pass beyond the cecum. In a series of 1,500 cases in which a barium enema was given Case reported 250 instances of insufficiency. Other values are those cited by Hammer (70 per cent), Herlyn (42 per cent), Alvarez (60 per cent), Carman (90 per cent), Dietlen (20 per cent) and Cole (33 per cent). This variance in values must indicate a variance in technic in the administration of the barium enemas. It is reasonable to assume that the higher the pressure utilized the greater the percentage of instances of incompetency. At the University Hospital it has been estimated by Dr. Rigler that in approximately 80 to 90 per cent of all the cases in which barium enemas are given, incompetency of the sphincter is shown.

Most investigators have found that the sphincter is competent to withstand moderate increases of intra-enteric pressure. Rost stated "In general, the valve prevents backflow from the large intestine and also remains closed when the pressure there is fairly high, as for example, in large intestinal ileus." Despite reports by roentgenologists on the relative insufficiency of the sphincter, the fact remains that in clinical cases of obstruction of the large bowel the condition is often observed to progress to gangrene of the cecum and perforation without evidence of dilatation of the small bowel. In an attempt to correlate these paradoxical statements the following observations are presented:

- 1 Pressures utilized in barium enemas produce sudden massive filling of the colon and are much higher than any which might occur even in cases of extreme obstruction. Filling of the colon in a case of obstruction is gradual. Forty millimeters of mercury (52 cm of water) is the highest pressure I have measured in clinical cases of obstruction.

- 2 The pressure exerted by the barium enema is usually greatly augmented by manual manipulation of the cecum.



3 Barium enemas are usually given to persons while fasting, in which state, according to Tonnis, the sphincter is most likely to be incompetent

4 The greatest percentage of barium enemas are administered to younger persons with a normal colon. The results cannot be applied to the pathologic colon subjected to gradual distention and increase of intra-enteric pressure, which must certainly, by irritation of the cecal mucous membrane, affect the tone of the ileocecal sphincter

### EXPERIMENTAL WORK

Experimental work was undertaken to ascertain (1) whether the ileocecal sphincter is competent to withstand pressures which occur clinically in the colon, (2) whether irritation of the distal portion of the colon or of the ileocecal nerves will increase the tone of the ileocecal sphincter and make it competent to withstand higher pressures and (3) whether increase of intra-enteric pressure to the limits observed clinically will result eventually in damage to the wall of the bowel sufficient to account for the clinical complications of gangrene, perforation and peritonitis. Clinical observations are reported of pressures that obtain in cases of obstruction of the large bowel

#### STUDY OF COMPETENCY OF THE ILEOCECAL SPHINCTER IN CADAVERS

In the cadaver the ileocecal sphincter acts only mechanically, owing to the loss of tone. I shall refer to it as a "valve" in this section only. Throughout the remainder of the paper it will be referred to as a "sphincter."

The ileocecal portion of the bowel was obtained from 4 cadavers at autopsy. One specimen, obtained six hours after death, proved incompetent to withstand air injected through the ileum or colon. The second specimen, taken from a person who had died two hours before, was entirely competent (air could not be forced backward into the ileum under pressures of more than 144 mm of mercury). Under this pressure, owing to distention of the colon, the air began to seep through the wall. Injection of air through the ileum under a pressure of 64 mm overcame the resistance of the valve. Repeated attempts to inject air into the colon showed that the valve was competent to resist a pressure of 140 mm. In the third specimen, obtained two hours after death, a colo-ileal regurgitation was obtained at a pressure of 32 mm, and ileocolic insufficiency, at a pressure of 14 mm. In the fourth specimen, four hours after death, colo-ileal regurgitation was obtained at a pressure of 20 mm, and ileocolic insufficiency, at a pressure of 10 mm.

It would appear from these few studies on cadavers and from the literature already cited that observations on a cadaver are of no value, because, first, tone is an important factor in the competency of the

valve, as it acts like a true sphincter, and, second, competency of the valve in a cadaver would depend entirely on the degree of coaptation of the lips of the valve at the time of death

#### TESTS OF COMPETENCY OF THE ILEOCECAL SPHINCTER IN DOGS

Dog 1—With ether anesthesia, 1 foot (30-48 cm) of intestine was isolated on either side of the ileocecal junction and clamped with rubber-covered intestinal clamps. A T-tube cannula was inserted into the ileum and into the cecum 12 inches (30-48 cm) distal to the sphincter, and one end was connected to a mercury manometer

1 One hundred cubic centimeters of air was slowly injected into the ileum. The ileum was distended until a pressure of 70 mm of mercury was reached. At this pressure the ileocecal sphincter suddenly relaxed and allowed air to enter the cecum.

2 The preceding experiment was repeated the cecum being gradually filled with air until a pressure of 76 mm was reached when the sphincter became incompetent and allowed air to rush into the ileum.

3 Air injected into the ileum passed the sphincter only when a pressure of 72 mm of mercury was reached. The colon became distended. When the ileum was suddenly decompressed the colon remained distended at a pressure of 15 mm, with the sphincter still competent. It was necessary to increase the pressure in the colon to 80 mm again before the sphincter gave way and allowed air to pass into the ileum.

Dog 2—Similar experiments were repeated at intervals of thirty minutes. The following results were obtained:

1 Ileocolic insufficiency appeared at a pressure of 54 mm and colo-ileal regurgitation, at a pressure of 42 mm.

2 Ileocolic insufficiency was obtained at a pressure of 30 mm, and colo-ileal regurgitation, at a pressure of 32 mm.

3 Ileocolic insufficiency was obtained at a pressure of 40 mm and colo-ileal regurgitation, at a pressure of 32 mm.

When the ileum was suddenly decompressed the sphincter held air in the colon under a pressure of 20 mm of mercury.

Dog 3—A T-tube cannula was inserted into the ileum, and a rectal tube was inserted into the colon through the anus and secured by a purse string suture. Air was injected through the rectal tube until a pressure of 226 mm of mercury was recorded in the colon. At this pressure the sphincter evidently gave way, and air rushed into the ileum. Repetition of this experiment in thirty minutes gave the same result at a pressure of 60 mm. After this, complete paralysis of the sphincter ensued, the two systems acting as one.

In the rest of the experiments the effect of electrical stimulation with the induction coil of the splanchnic nerves (ileocolic vessels and the ileocolic nerve), the distal portion of the colon, the small bowel and other viscera was noted.

Dog 4—Colo-ileal regurgitation occurred at a pressure of 36 mm of mercury. When the ileo-colic vessels were stimulated the resistance of the sphincter was increased until it equaled a pressure of 124 mm. This test was repeated, and still

the resistance of the sphincter was equal to a pressure of 64 mm, almost twice that of the normal sphincter

Dog 5—Colo-ileal regurgitation occurred at a pressure of 40 mm of mercury. When the distal portion of the colon was stimulated the resistance of the sphincter was equal to a pressure of 120 mm. In thirty minutes a redetermination of the normal resistance to colo-ileal regurgitation showed it to be equal to a pressure of 64 mm. On stimulation of the ileocolic vessels the resistance increased until it equaled a pressure of 107 mm.

Dog 6—Colo-ileal regurgitation occurred at a pressure of 88 mm. When the distal part of the colon was stimulated the resistance of the sphincter was increased to withstand a pressure of 112 mm. The normal resistance was determined again and was found to be equal to a pressure of 66 mm. On stimulation of the ileocolic vessels a reading of 124 mm was obtained before the sphincter gave way.

Dog 7—Colo-ileal regurgitation occurred at a pressure of 60 mm. When the ileocolic vessels were stimulated the resistance to regurgitation was equal to a pressure of 114 mm. The normal resistance determined after thirty minutes was equal to a pressure of 50 mm. On stimulation of the distal portion of the colon resistance to regurgitation increased to withstand a pressure of 120 mm.

Dog 8—The normal resistance to regurgitation was equal to a pressure of 70 mm. The resistance when the stomach was stimulated was still equal to a pressure of 70 mm. The normal resistance was again determined and found to be equal to a pressure of 76 mm. The resistance when the parietal peritoneum was stimulated was equal to a pressure of 80 mm. The normal resistance was equal to a pressure of 70 mm. On stimulation of the colon the resistance was equal to a pressure of 200 mm. Practically no change in the resistance to regurgitation was observed, except when the colon was stimulated.

A series of experiments on a cat was performed. Similar results were obtained as follows: The resistance to colo-ileal regurgitation under normal conditions was equal to a pressure of 70 mm of mercury, on stimulation of the peritoneum, to 65 mm, of the colon to 78 mm, of the ileocolic vessels, to 140 mm, of the appendix, to 100 mm, of the small bowel, to 50 mm, and of the colon, to 140 mm. The normal resistance again determined was equal to a pressure of 60 mm.

It is evident from these experiments that the ileocecal sphincter of the dog and cat is competent to withstand pressures of from 60 to 80 mm of mercury. This normal resistance has a constant value for each animal, as shown by many repeated tests, and it is greatly increased by stimulation of the sympathetic nerves and by irritation of the serosa of the distal part of the colon. Stimulation of the parietal peritoneum of other viscera had no such effect. Stimulation of the colon must enhance the tone of the ileocolic sphincter through Auerbach's plexus. A similar observation was made by Short, who noted a decrease of ileocolic inflow when he stimulated the cecal mucosa. It is significant that even the normal resistance of the sphincter to colo-ileal regurgitation is much higher than any increased pressure noted in clinical cases of obstruction of the large bowel.

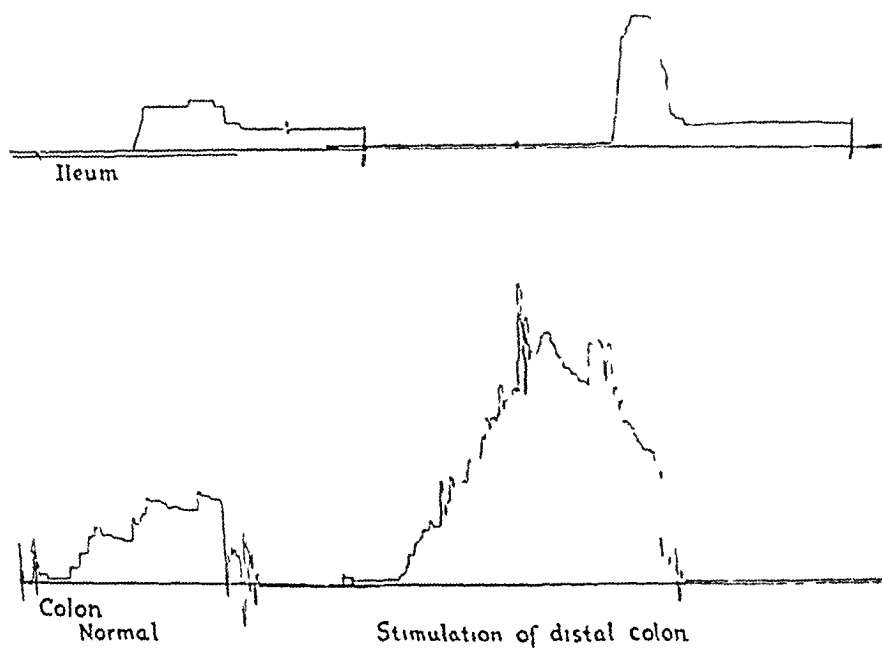


Fig 1 (dog 5) —Increased competency of the ileocecal valve on stimulation of the distal portion of the colon

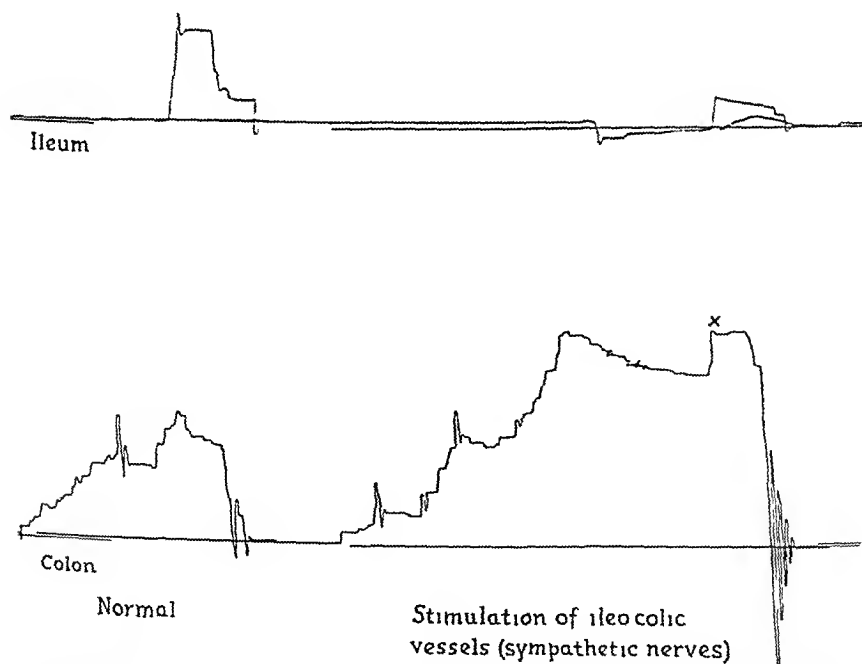


Fig 2 (dog 7) —Increased competency of the ileocecal valve on stimulation of the ileocolic vessels (sympathetic nerves)

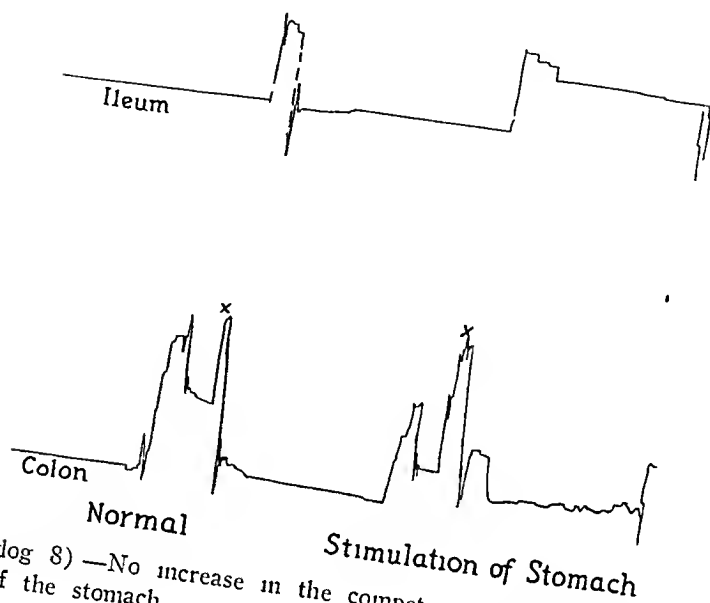


Fig 3 (dog 8) —No increase in the competency of the ileocecal valve on stimulation of the stomach

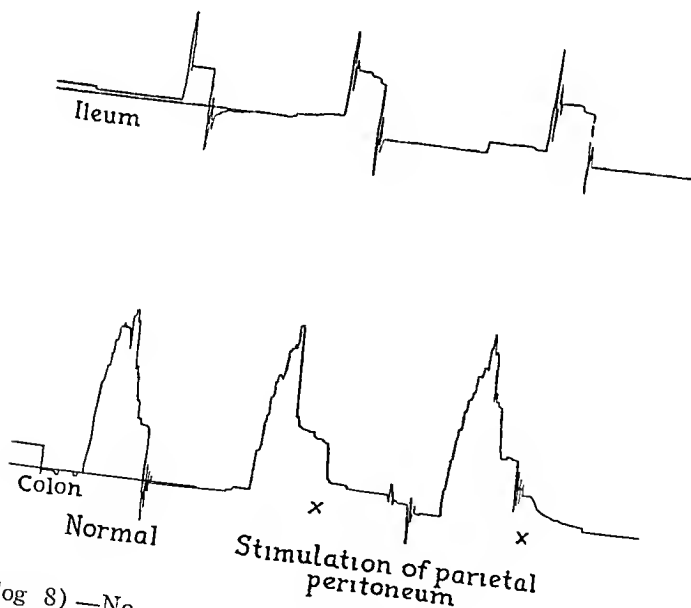


Fig 4 (dog 8) —No increase in the competency of the ileocecal valve on stimulation of the parietal peritoneum

TESTS OF COMPETENCY OF THE ILEOCECAL SPHINCTER IN MAN BY  
INSUFFLATION OF AIR UNDER LOW PRESSURE AND BY  
THE ADMINISTRATION OF BARIUM ENEMAS

With the cooperation of Drs. Rigler and Borman of the department of roentgenology of the University Hospital, it was observed that with the usual technique with a pressure of gravity of 3 feet (91.44 cm) of barium (from 80 to 100 mm of mercury) and with manipulation of the abdominal wall it was possible to render the ileocecal sphincter incompetent in a high percentage of persons. The competency of the human sphincter was tested under a lower pressure, 50 mm of mercury or 2 feet (60.96 cm) of barium. In a series of subjects the colon was first gradually distended with air until the cecum was well visualized under the fluoroscope. The barium was injected under a pressure of gravity of 50 mm. It was observed that the colon was much more difficult to fill with barium if air had previously been injected. This was interpreted as due to the competency of the ileocecal sphincter to withstand the compression of the air present in the cecum. In 5 cases the ileocecal sphincter was competent even after manipulation. In 3 instances the barium passed easily into the small bowel. In 1 case barium entered the ileum under a pressure of only 1 foot (30.48 cm) of barium (30 mm of mercury). In 5 other cases the barium was seen to pass through the sphincter, but only after prolonged delay. It is evident that, owing to individual differences, a large series would be necessary on which to base conclusions, and it is doubtful whether the values obtained by Case (250 instances of insufficiency in a series of 1,500 cases in which barium enemas were given) could be approached. There must be a fundamental difference between the response of the ileocecal sphincter to the sudden massive filling with barium and that to the gradual distention with gas and feces which occurs in cases of obstruction of the large bowel.

SIGNIFICANCE OF THE COMPETENCE OF THE ILEOCECAL  
SPHINCTER IN CASES OF COLONIC OBSTRUCTION

## REPORTS OF CASES

The best proofs of competency of the ileocecal sphincter in cases of obstruction of the large bowel are the instances reported of gangrene and perforation of the cecum which occur in association with stenosis due to carcinoma of the sigmoid flexure. The German literature is replete with reports of cases in which the colon was greatly distended and gangrenous while the ileum was empty. Shimodaira presented 48 cases of his own and referred to the reports of Albarran and Lavillaunoy, Labey, Letulle, Kochei, Kreuter, von Greyerz and others, who have mentioned cases or have referred to instances of ulceration gangrene

or perforation of the cecum resulting from obstruction Reichel reported 12 instances of perforation in a series of 216 cases of carcinoma of the colon Eight of these perforations were in the cecum Nielson reported 2 in a series of 87 cases of carcinoma of the colon Cohen reported 2 cases Ginzburg recently noted that "even in cases of long-standing obstruction of the colon, dilated small bowel and fluid levels are not visualized by X-ray"

I wish to report 4 illustrative cases

*CASE 1—History and Course*—H H, a white man aged 63, was admitted to the University Hospital on Aug 30, 1931 He gave a history of gradual loss of weight for a period of six months, during which there had been attacks of pain in the abdomen Distention and acute abdominal pain were present three days before admission, and vomiting began two days before Examination of the abdomen at the time of admission revealed definite distention but no rigidity or tenderness either before or on rebound Auscultation of the abdomen revealed the presence of loud borborygmi about the umbilicus and in the right lower quadrant On rectal examination a small mass was palpated high in the left side Roentgen examination of the abdomen showed marked distention of the large bowel with gas and the presence of levels of fluid Because of apparent dehydration and the poor condition of the patient, it was thought best to defer operation for a few hours, during which 3,000 cc of saline solution was administered subcutaneously One and one-half hours before operation the patient experienced acute pain in the right lower quadrant Examination at this time showed rigidity and tenderness both before and on rebound on the right side, neither of which signs was present at the time of admission six hours before These findings suggested at once the presence of gangrene or perforation of the cecum There was no obliteration of hepatic dulness on percussion

*Operation*—A large amount of turbid fluid was present in the peritoneal cavity The cecum was enormously distended, there was no distention of the small bowel Several rents in the cecal wall extended through the serosa and the muscularis, through which herniation of the mucosa had occurred One of these tears measured 6 inches (15.24 cm) The mucosa was greenish-black, suggesting gangrene extending through the entire thickness of the intestinal wall Cecostomy was performed, and the abdomen was closed

*CASE 2—History and Course*—A H, a white man aged 73, was admitted to the University Hospital on March 25, 1932, complaining of abdominal pain, distention, vomiting and anorexia of several days' duration He was in such poor general condition that it was impossible to ascertain the actual duration of his complaint Examination revealed marked distention of the abdomen Peristalsis was visible through the abdominal wall At intervals loud borborygmi were audible, and many metallic tinkles were heard Slight diffuse tenderness on palpation was present, but rigidity and tenderness on rebound were absent There were no palpable masses, and the results of rectal examination were negative The nonprotein nitrogen content of the blood was 57 mg per hundred cubic centimeters and the chloride content, 585 mg Roentgenograms of the abdomen revealed enormous distention of the colon The clinical diagnosis was obstruction of the large bowel, due probably to neoplasm of the colon on the left side Fourteen hundred cubic centimeters of a dextrose and saline solution was given subcutaneously By gastric lavage only 50 cc of bloodstained fluid was obtained

*Operation*—The abdomen was opened through a right McBurney incision. A markedly distended colon was presented. No distention of the small bowel was visible, the terminal portion of the ileum being collapsed. A needle connected to a mercury manometer was inserted into the colon, and the intra-intestinal pressure was determined to be 27 mm of mercury (35 cm of water). Eighteen hundred cubic centimeters of gas was drawn off immediately through the needle until the recorded pressure was only 4 mm of mercury (5 cm of water). The needle puncture in the wall of the bowel was closed by suture. Examination revealed the presence of a sigmoid carcinoma in the lower part of the sigmoid flexure. Sigmoidostomy was carried out. It was thought advisable to perform



Fig 5 (case 1) —Roentgenogram of the abdomen, showing marked distention of the large bowel with gas in a case of acute obstruction of the large bowel of three days' duration, due to carcinoma of the sigmoid flexure. Distention of the cecum is the most prominent feature with no distention of the small bowel. (From Wangenstein, O. H., and Paine, J. *Treatment of Acute Intestinal Obstruction by Suction with the Duodenal Tube*, J. A. M. A. **101** 1532 [Nov. 1] 1933, fig. 1.)

also a cecostomy or an appendicostomy, but the cecum could not be delivered. Therefore, ileostomy was carried out, and the abdomen was closed. The patient subsequently died.

*Autopsy*—The gastro-intestinal tract presented a remarkable picture. The entire large bowel was markedly distended to a diameter of approximately 12 cm. Obstruction was due to carcinoma of the sigmoid flexure. A carcinomatous ulcer 5 cm in diameter occurred at the point of constriction. The colon itself weighed 1,750 Gm and contained 4,050 cc of fluid. There were marked hypertrophy and



thickening of the wall of the entire large bowel. The ileocecal valve was competent to withstand back pressure. The small bowel was not dilated. However, there was definite evidence of hypertrophy of the wall. The hypertrophy was more evident near the ileocecal valve, the wall of the jejunum showing no signs of increased thickening.

*CASE 3—History and Course*—H. J., a white man aged 53, was admitted to the University Hospital on Nov. 19, 1933. The history dated from 1931, at which time he was operated on at another hospital for the relief of acute obstruction of the large bowel. Details of the operation are unknown. On admission he complained of severe, colicky, intermittent abdominal pain and complete obstipation of four days' duration. Alternating diarrhea and constipation had been present for several days prior to the onset of acute symptoms. There was increasing distention. He had vomited only once on the day before admission. Examination revealed prominent distention and both visible and audible peristalsis. A roentgenogram of the abdomen revealed marked distention of the colon. Water used in lavage of the stomach was returned clear. No gas or fluid was obtained. Nasal suction was instituted with no relief.

*Operation*—Cecostomy was carried out through a right McBurney incision. A mass was palpated in the sigmoid flexure. Intra-enteric pressure (in the cecum) at the time of cecostomy was 18 mm of mercury. Pressure was maintained at 10 mm (13 cm of water). The intestinal wall was edematous. There was marked congestion of the mesenteric veins. Profuse bleeding occurred from the puncture wound of the needle, indicating high venous and capillary pressures. Three hundred cubic centimeters of gas was removed by suction through the needle, and the cecum was exteriorized for cecostomy. Four hours later the pressure in the exteriorized bowel had increased to 40 mm (52 cm of water). The bowel was opened, a no. 24 catheter was inserted into the proximal loop, and by alternate suction and irrigation the distention was successfully reduced.

*CASE 4—History and Course*—Mrs. A. G., a white woman aged 72, was admitted to the University Hospital on Jan. 27, 1933, with a history of attacks of diarrhea, vomiting and abdominal pain of one month's duration. The stools had frequently been black. Obstipation, colicky abdominal pain and progressive abdominal distention had been present for three days. There had been no vomiting in the twenty-four hours prior to admission. Examination revealed marked distention of the abdomen, visible and audible peristalsis and moderate tenderness in the lower portion of the abdomen. On rectal examination a mass of questionable character was noted high in the left side, which seemed to be extrinsic to the bowel. Proctoscopic examination of the colon for 17 cm gave negative results. Roentgenograms of the abdomen revealed distention of the large bowel only.

*Operation*—Cecostomy was performed. The entire colon, especially the cecum, was distended. Exploration failed to reveal the obstructing mechanism. The intra-enteric pressure was determined to be 12 cm of water. The post-operative course was complicated by an attack of coronary thrombosis and auricular fibrillation. On the twelfth postoperative day the temperature increased to 102 F, the pulse became thready, and the patient complained of dyspnea, which was relieved by the administration of oxygen. No abdominal abnormalities were noted. Death occurred on the sixteenth postoperative day.

*Autopsy*—Examination of the gastro-intestinal tract revealed edema of the wall of the lower portion of the ileum as one approached the ileocecal valve. There was no obstruction of the small bowel. The entire colon was moderately

dilated as far as the sigmoid flexure. The intestinal wall was much thickened and edematous. Three large perforations of the colon were evident each approximately 4 cm in diameter. One occurred in the transverse colon, 1 in the splenic flexure and 1 in the sigmoid flexure at the brim of the pelvis. The edges of the defects were black and appeared necrotic. The peritoneal cavity was filled with feces and showed signs of fecal peritonitis. On opening the colon the mucosa of the cecum and ascending colon was observed to be reddened and edematous. Beginning at the hepatic flexure irregular patches of ulceration involved the mucosa and submucosa. At the splenic flexure and in the descending colon these patches fused into an almost continuous extremely irregular area of ulceration. About 30 cm above the anus a small adenocarcinoma had completely occluded the bowel.

*Diagnosis*—The final diagnosis was carcinoma of the sigmoid flexure with intestinal obstruction and secondary ulceration and perforation of the intestinal wall and fatal peritonitis. The question of the etiology of the perforation and

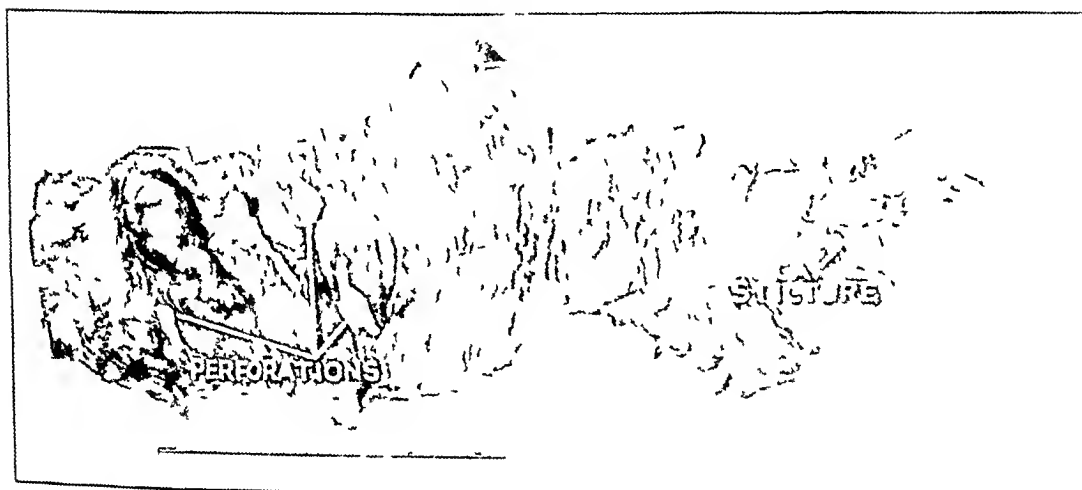


Fig 6 (case 4)—Photograph of a postmortem specimen of the colon showing extensive ulceration and three large perforations

ulceration is difficult to settle. The conditions are probably explained on the basis of fecal impaction, stercoral ulcers and damage to the circulation of the wall of bowel by the increased intra-enteric pressure. It is possible that the ulceration and perforation were the result of inadequate drainage of the colon, that is, the cecostomy opening was not large enough to decompress adequately the distal part of the colon and empty it of feces. Sections of the intestinal wall studied by parasitologists did not reveal *Amoeba*. The diagnosis of acute ulcerative colitis on the basis of inflammation above the site of obstruction cannot be ruled out. Labey, Letulle and most recently Reichel have advanced this hypothesis.

#### EFFECT OF INCREASED INTRA-ENTERIC PRESSURE ON THE WALL OF THE BOWEL

Pathologic changes in the intestinal wall as a consequence of increased intra-enteric pressure must be secondary to the effect on the circulation of the wall of the bowel. Kocher was the first to recognize the signifi-

cance of increased intra-enteric pressure. He noted that distended incarcerated hernial loops had a congested appearance and that when gangrene appeared it was located on the antimesenteric border. He observed the so-called *Dehnungsgeschwüre* (distention-induced ulcers) and ascribed their occurrence to the effect of distention on the circulation of the wall of the bowel.

Shimodaira, a pupil of Kocher, collected 48 instances of perforation and rupture of the intestinal wall due to obstructing strictures, i. e., to carcinoma of the colon. He distended closed loops of the bowel of dogs with air until they appeared anemic. Death usually followed in three or four days. In 3 cases perforated ulcers were revealed at postmortem examination. All the loops were congested, and most presented areas of gangrene on the antimesenteric border. His explanation of the pathogenesis of these changes was that distention produces stasis in circulation, which results in thrombosis, ecchymosis, hemorrhagic infiltration of the submucosa and ulceration of the mucosa and eventually in perforation. Von Greyerz ascribed the congestion of the bowel to paralysis of the vasomotor apparatus, at first intermittent, owing to peristaltic rushes, but later constant.

Many American workers have referred to the obvious disturbance of circulation and the consequent impairment of function of the intestine as a result of increased intra-enteric pressure. Van Zwahlenburg studied the effect of distention on the blood flow through the intestinal wall by means of an electric bulb within the lumen. He noted that at a pressure of 30 mm. of mercury there was capillary stasis, at 60 mm., venous stasis, at 90 mm., partial arterial arrest, and at 130 mm., complete arrest of the circulation. Gatch, Trusler and Ayers inserted cannulas into the mesenteric veins returning from closed loops and measured the volume of flow per minute under experimentally increased intra-enteric pressures. They found that for each increase of pressure there was a corresponding decrease in blood flow. Dragstedt, Lang and Millet repeated this experiment, using different levels of the gastro-intestinal tract, and found that the circulation of the duodenum was more profoundly affected than that of any other portion of the bowel. That there is disturbance of circulation in the distended bowel was confirmed recently by Jacques and his associates, who made studies of the surface temperature of the distended bowel above the site of strangulated obstruction and found the temperature to be uniformly decreased.

Van Zwahlenburg attempted to explain the pathologic changes occurring in cases of intestinal obstruction on the basis of anoxia of the tissues of the intestinal wall. According to this worker, stasis of blood in the wall of the distended bowel results in a decreased supply of oxygen, which affords excellent opportunity for development of infection and its

sequelae—gangrene, necrosis and perforation. There can be no doubt that at least partial asphyxia of the wall occurs. McClure showed that the stagnant contents of obstructed loops form excellent culture mediums for growth of bacteria. The bacteria invade partially asphyxiated tissues of the intestinal wall with resulting pathologic changes. Downes showed that venous stasis is conducive to invasion by leukocytes. This would explain the infiltration of the wall of the bowel with polymorphonuclear and mononuclear cells.

Van Beuren presented a plausible explanation for the occurrence of pathologic changes in the intestinal wall in cases of obstruction. He observed that the characteristic features of the pathologic picture were areas of hemorrhagic infarction on the antimesenteric surface of the intestine and varying degrees of necrosis culminating in perforation in cases of long-standing lesions. His explanation of the infarction of the wall of the bowel is based on purely mechanical factors. With distention the size of the bowel is increased to three times the original diameter, which results in marked thinning of the wall and in compression and decrease in the size of the lumen of the small blood vessels of the wall. The vessels elongate to accommodate the increased circumference, and this further reduces the size of their lumens. Owing to the increased intracapillary pressure and the pressure from within the bowel the smallest vessels at the antimesenteric border rupture producing hemorrhagic infarcts and subsequent necrosis and perforation.

#### EXPERIMENTAL WORK

The following experiments were undertaken to ascertain what effect constant pressures of from 30 to 50 cm. of water (present in cases of obstruction of the large bowel) have on the intestinal wall.

Dog 1—With the animal under pentobarbital sodium anesthesia a rectal tube was inserted into the rectum of a dog and secured by a purse-string suture about the anus. Laparotomy was then performed, and a purse-string suture was placed about the lower part of the ileum. The abdomen was closed, and the colon was inflated through the rectal tube under a constant pressure of 30 cm. of water maintained for twenty-four hours by the use of the Perusse bottle. The dog was then killed. At autopsy the colon showed congested areas in the mucosa, small petechial hemorrhages in the serosa and interstitial hemorrhage in the muscle layers with infiltration of round cells in all the layers (fig. 7A).

Dog 2—The experiment was repeated, this time the colon being subjected to a pressure of 50 cm. of water. After twenty-four hours pneumoperitoneum was present. At autopsy marked congestion and areas of hemorrhagic necrosis were evident, especially in the cecum and appendix. The ileocecal sphincter was not competent to withstand this sustained pressure, and distention of the ileum had resulted in perforation through an area of hemorrhagic necrosis.

From this study it is evident that a pressure of from 30 to 50 cm. of water, if sustained for a sufficient period, will produce marked patho-

logic changes in the intestinal wall, such as are noted in clinical cases of obstruction of the large bowel. It is conceivable that lower pressures of from 10 to 20 cm of water, if constantly maintained, could produce similar changes over a longer time.

The importance of increased intra-enteric pressure in the development of pathologic changes in the wall of the bowel might be minimized for two reasons. First the pressures recorded in cases of experimental obstruction are comparatively low, and, second, the bowel can readily

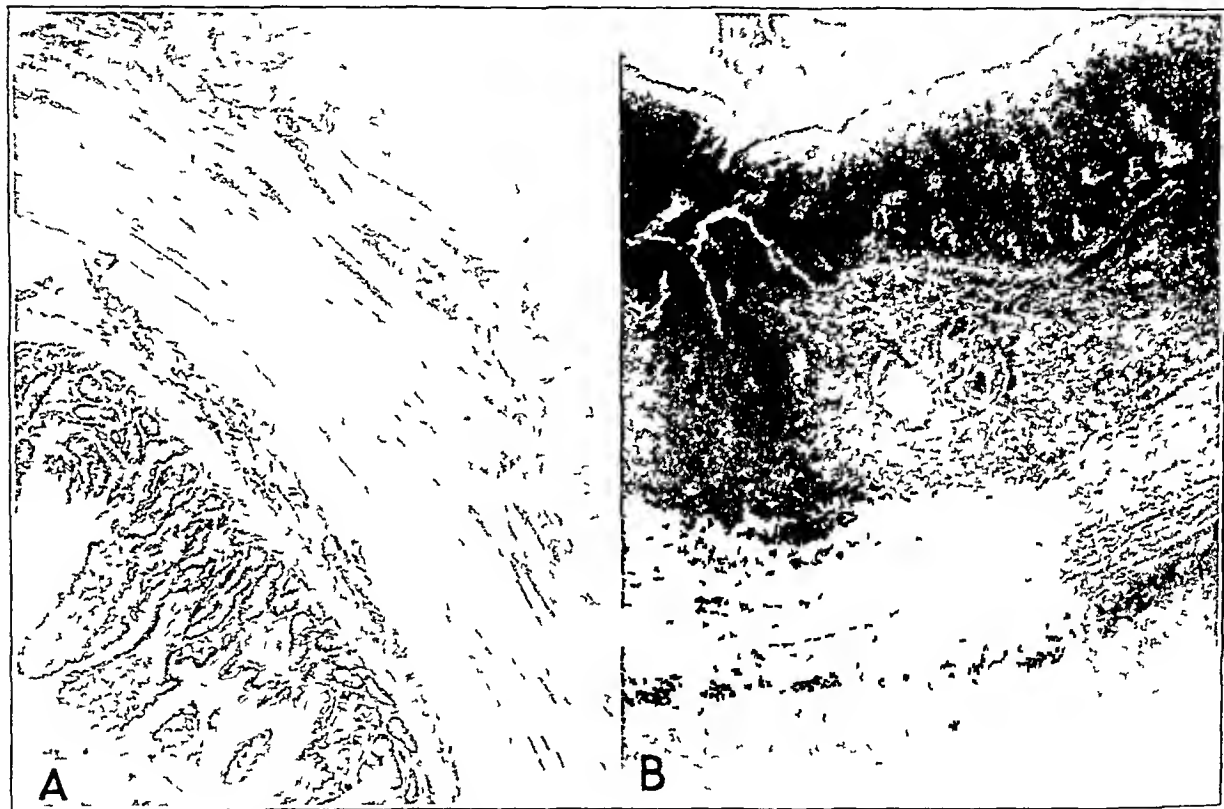


Fig 7—Photomicrographs of the wall of the colon (A) of dog 1, subjected to a pressure of 30 cm of water for twenty-four hours, showing areas of hemorrhagic infiltration, especially in the muscularis and subserosa, and (B) of dog 2, subjected to a pressure of 50 cm of water for twenty-four hours. The areas of hemorrhagic infiltration and necrosis throughout all the layers of the wall of the bowel are to be noted. The section is taken from the antimesenteric border.

accommodate itself by compensatory dilatation to slight changes in intra-enteric pressure. However, that this is not the case is illustrated by the fact that a pressure of 10 cm of water, if constantly maintained over a sufficient period (twenty-four hours) will produce areas of hemorrhagic necrosis in closed ileal loops (unpublished thesis for the degree of Doctor of Philosophy).

There is probably a difference between the effect on the intestinal wall of sustained pressure and that of intermittent pressure, even if the intermittent pressure is high. During normal peristaltic rushes there is no doubt that high pressures obtain, but they do not damage the intestinal wall, even though temporary contraction may be sufficient to cause anemia, i. e. blanching of the wall of the bowel, because ample opportunity is afforded the intestinal wall to return to the normal state in the interval between contractions. This interval during which the wall is free from pressure is lacking, of course, when the intra-enteric pressure is sustained at a definite level. Undoubtedly, this holds true in cases of obstruction. That pathologic changes are not more often seen in the wall of the bowel is due to the ability of the bowel to relax and accommodate itself to increased intra-enteric pressure. This is especially true in cases of simple obstruction. In cases of the closed loop this phenomenon no doubt also occurs but it is evident that at some point the sustained intra-enteric pressure must increase bringing with it the possibility of strangulation when a sufficiently high level of constant pressure is attained.

#### MEASUREMENT OF THE INTRA-ENTERIC PRESSURE IN CASES OF OBSTRUCTION OF THE LARGE BOWEL

A great many observations have been recorded of the increased intra-enteric pressure in cases of experimental obstruction of the small intestine. Owings, McIntosh, Stone and Weinberg have determined experimentally that the normal sustained intra-intestinal pressure in dogs is from 2 to 4 cm. of water. In simple obstruction of the ileum they found that the sustained pressure was increased to 8 cm. of water and during activity of the bowel it rose to as high as from 30 to 60 cm. (approximately from ten to fifteen times the normal pressure). Buiget and his associates, working with closed loops of the jejunum in dogs, found pressures varying from 30 to 60 cm. of water. The average high pressure was 39.5 cm. of water (30.4 mm. of mercury). Owings and his associates found pressures of as high as 70 cm. of water in closed loops. It is evident that the pressure in closed loops attains higher levels in shorter periods than those in cases of obstruction of the simple type, in which the bowel is afforded a chance to empty itself by reversed peristalsis and regurgitation.

Morton and Sullivan compared pressures in closed loops of the jejunum with those in similar loops of the ileum. They found that the intra-enteric pressure of the jejunal loop was 7 times that which developed in ileal loops (52 cm. of water as compared to 8 cm.). They attributed this difference to the fact that secretion is much more active in the jejunum than in the ileum. It is conceivable that pressure in the colon in cases of obstruction of its distal half would rise, owing to the

fact that its contents are constantly increased by fluids and gas from the ileum, which cannot be regurgitated because of a competent ileocecal sphincter

Stone and Frior obtained a pressure of 150 cm of water in a case of obstruction of the lower part of the ileum of several hours' duration. So far as I can determine, this is the only clinical measurement of intra-intestinal pressure which has been recorded in a case of intestinal obstruction in man. During the past few years I have had occasion to measure the intra-enteric pressure in patients with obstruction of the large bowel who have been admitted to the University Hospital. Measurements of pressure were also made in cases of carcinoma of the large bowel or the rectum in which colostomy was performed preliminary to resection. The intra-enteric pressure was determined just prior to the release of the clamps or to making the colostomy opening. Pressures varying from 10 to 50 cm of water were obtained.

*Measurements of Intra-Enteric Pressure in Clinical Cases of Obstruction of the Large Bowel*

No	Name	Diagnosis	Procedure	Duration of Obstruction	Pressure, Cm of Water
1	Baby B	Imperforate anus	Colostomy	60 hrs	12
2	Baby Br	Imperforate anus	Colostomy	18 hrs	10-26
3	R D	Carcinoma of the rectum	Colostomy	60 hrs	12
4	A S	Carcinoma of the rectum	Colostomy	72 hrs	18
5	E G	Carcinoma of the rectum	Colostomy	104 hrs	12-16
6	E C	Carcinoma of the rectum	Colostomy	80 hrs	13
7	C A	Carcinoma of the sigmoid flexure and acute obstruction	Cecostomy	8 days	23-26
8	A H	Carcinoma of the sigmoid flexure with obstruction	Cecostomy	?	35
9	J C	Carcinoma of the ascending colon with obstruction	Cecostomy	4 days	24
10	T W	Carcinoma of the rectum with obstruction	Colostomy	3 days	15
11	H J	Carcinoma of the sigmoid flexure with obstruction	Cecostomy	3 days	52
12	A G	Carcinoma of the sigmoid flexure with obstruction	Cecostomy	3 days	12

Six of the determinations of pressure noted in the table were made in cases of acute obstruction of the large bowel. In 4 cases obstruction was due to carcinoma of the sigmoid flexure, in 1, to carcinoma of the ascending colon, and in 1, to carcinoma of the rectum. The pressures were measured at the time of operation. In 4 instances of carcinoma of the rectum among the remaining cases colostomy was carried out as a procedure preliminary to resection. The colostomy opening was made only after definite clinical signs of obstruction (distention and colicky pain) became evident. In some of these cases roentgen examination preliminary to opening the bowel revealed only distention of the large

bowel It was noted that in the cases in which nasal suction was instituted after operation the patients were more comfortable and were able to tolerate the obstruction for a somewhat longer period However, in spite of suction definite distention of the large bowel developed in all the cases, owing no doubt to the fact that gas and chyme could pass into the cecum but could not be sucked out because of the competency of the ileocecal sphincter In 2 cases colostomy was performed for the correction of imperforate anus in a child The intra-enteric pressure was measured when signs of obstruction necessitated making the colostomy opening

It is to be noted that all these pressures are well below that employed by the roentgenologist to force the ileocecal valve They represent the level of sustained pressure within the bowel No doubt, higher pressures would be recorded during peristaltic rushes It is regrettable that no determinations of pressure were made in the case of gangrene of the cecum which is recorded as the first in this series

#### COMMENT

It has been shown that the ileocecal sphincter is competent to withstand pressures within physiologic limits (pressures of from 10 to 50 cm of water) which conceivably might occur in the course of obstruction of the large bowel A competent ileocecal sphincter at once converts a simple type of obstruction into a closed loop with all the inherent dangers of strangulation due to increased intra-enteric pressure Experimentally, the effect of such sustained pressures is shown by the development of areas of hemorrhagic necrosis in the colon of dogs That similar changes occur in the human colon is evident from a perusal of the literature cited and from the reports of cases in this paper

The term "ileocecal valve" is a misnomer, the organ is more rightly called the ileocecal sphincter It is subject to definite nervous control, and its competency depends on the tonicity of the fibers of the sphincter That the tone of the sphincter is increased by stimulation of the sympathetic nerves is confirmed by the experiments in this study Also, it has been shown that stimulation of the distal part of the colon increased the resistance of the sphincter to back pressure to approximately three times that of the normal sphincter Stimulation of the parietal peritoneum, the stomach or the small bowel had no such effect It is conceivable that the resistance of the ileocecal sphincter to back pressure is greatly increased in cases of intrinsic pathologic conditions of the colon Stimulation of the distal portion of the colon, acting through Auerbach's plexus increases the tone of the ileocecal sphincter, making it more competent



Several important clinical observations present themselves with relation to a competent ileocecal sphincter in cases of obstruction of the large bowel

1 Vomiting is a late symptom in cases of obstruction of the large bowel. The competent ileocecal valve allows material to pass into the colon but none to be regurgitated into the small bowel and stomach. Pain, distention and obstipation may be present for several days before the onset of vomiting. Vomiting may then be due to reflexes set up by distention of the colon (distention of any hollow viscus may produce vomiting). It is interesting to note that in the cases cited aspiration of the stomach resulted in the return of only a few cubic centimeters, in spite of the fact that these cases represented late stages of obstruction.

2 Nasal suction as a method of decompression is of little value in the treatment of acute obstruction of the large bowel with considerable distention.

In instances of obstruction of the colon on the left side in which the distention has not been great, the employment of nasal suction will frequently permit one to attack the obstruction directly after subsidence of the obstructive features. The virtue of decompression by the duodenal tube in these cases lies essentially in the fact that aspiration of swallowed air and fluid from the upper portion of the intestinal canal and stomach prevents increase in the distention. As already noted, when the method is employed in this manner in cases of postoperative obstruction the appearance of obstructive symptoms and distention was delayed, allowing one to defer making the colostomy opening for several days.

3 A single roentgenogram of the abdomen of a patient with clinical intestinal obstruction should differentiate between obstruction of the small bowel and that of the large. Roentgenographic findings of a markedly distended colon and dilatation of the cecum with no visible loops of small bowel should clinch the diagnosis of obstruction of the sigmoid flexure. Roentgenography is the only accurate method of determining the degree of distention and the segment of bowel involved.

4 All acute obstructions of the large bowel exhibiting considerable distention should be treated as obstructions of the closed loop type with potential strangulation, by means of operative decompression (cecostomy). Simple mechanical obstruction of the small bowel has been treated successfully at the University Hospital by decompression by means of nasal suction (Wangensteen). This method, of course, is impossible in cases of the variety found in the large bowel, owing to the presence of a competent ileocecal sphincter. Adequate decompression by cecostomy should be carried out in cases of great distention to prevent, if possible, the complications resulting from continuous

increased intra-enteric pressure, i. e., gangrene and perforation of the intestinal wall. Patients who present only partial or low grade obstruction of the colon can be prepared for operation by medical management, and further distention of the colon can be prevented by the use of siphonage by nasal suction.

### CONCLUSIONS

The ileocecal sphincter is competent to withstand moderate increases of intra-enteric pressure, such as occur in cases of obstruction of the large bowel.

Obstruction of the colon with considerable distention is of the closed loop type, because the presence of a competent ileocecal sphincter effectually prevents regurgitation into the ileum.

The intra-enteric pressure which obtains in cases of obstruction of the large bowel has been measured in clinical cases and has been found to vary from 10 to 50 cm of water.

When the colon of the dog is exposed to a constant pressure of from 30 to 50 cm of water for a sufficient period (twenty-four hours) areas of gangrene and hemorrhagic necrosis appear in the wall of the bowel.

The clinical cases cited illustrate some of the aforementioned facts.

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# MARCH FOOT ASSOCIATED WITH UNDESCRIBED CHANGES OF THE INTERNAL CUNEIFORM AND METATARSAL BONES

I H MASERITZ, M D

BALTIMORE

For many years march foot was closely linked with the soldier, and the earlier literature was derived, almost in its entirety, from cases which had been seen in the ranks of the German and French armies. It is by no means a condition confined entirely to the soldier, but one that is seen less frequently in civilian life. For some years comparatively little attention was given to the subject, almost nothing was written, and it literally passed into obscurity. It is not surprising that many physicians today possess little or no knowledge of the condition, and it is more than likely that numerous cases have escaped recognition. In recent years Jansen<sup>1</sup> and others have again brought this subject to light. Undoubtedly interest has been stimulated, and much more should now be added to the chapter on marching fractures.

The primary purpose of this paper is to deal with several undescribed changes in march foot, but I feel that in conjunction with this a thorough discussion of the subject will not be out of place.

Breithaupt<sup>2</sup> described a swelling of the feet that commonly occurred in soldiers after a long march. He named this condition *Fussgeschwulst* and attributed it to an inflammation of the tendon sheaths. Weisbach<sup>3</sup> did not agree with the explanation of Breithaupt but felt that the changes responsible were those of an inflammation involving the ligaments and therefore applied the term *syndesmitis metatarsea*. Pauzat<sup>4</sup> described the condition as an edematous swelling of the feet, apparent on the dorsal and plantar aspects, and consisting of two stages, the first a simple soft tissue swelling and the second a periosteal proliferation. He further wrote that the second, third and fourth metatarsal bones were

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1 Jansen, Murk. Die Fussgeschwulst und ihre Ursache, *Ztschr f orthop Chir* **35** 8, 1916. March Foot, *J Bone & Joint Surg* **8** 262 (April) 1926.

2 Breithaupt. Zur Pathologie des menschlichen Fusses, *Med-Ztg* **24** 169 and 175, 1855.

3 Weisbach. Die sogenannte Fussgeschwulst (*Syndesmitis metatarsea*) des Infanteristen. *Deutsche mil-arztl Ztschr* **6** 551, 1877.

4 Pauzat, J E. De la periostite osteoplastique des metatarsiens a la suite des marches. *Arch de med et pharm mil* **10** 337 1887.

found to be tender and were the only bones that ever displayed changes. He considered these changes to be the result of an osteoplastic periostitis. Poulet<sup>5</sup> viewed the condition as a rheumatic osteoperiostitis. Martin<sup>6</sup> reported three types, one which was a simple periostitis, a second in which tendonitis alone existed, and a third that was described as a periostitis complicating mediotarsal arthritis. Busquet,<sup>7</sup> on the other hand, thought that there were three distinct groups of *Fussgeschwulst* (1) a direct periostitis, (2) an indirect periostitis and (3) a diathetic periostitis.

With the advent of the x-ray, Stechow<sup>8</sup> described the first cases of march foot that were studied roentgenologically. He demonstrated that march foot not only showed involvement of the periosteum but very frequently fractures, and he presented 34 cases with a single and 1 case with a double fracture. The frequency of involvement was as follows: first metatarsal bone, left foot, 0, and right foot, 0, second, left foot, 1 and right foot, 0, third, left foot, 11, and right foot, 8, fourth, left foot, 8, and right foot, 6, fifth, left foot, 0, and right foot, 0.

Schulte<sup>9</sup> reported 53 cases of *Fussgeschwulst*, which involved the second metatarsal bone in 33 instances, the third in 18 and the fourth in 2. The first and fifth metatarsal bones were never involved, and he considered each case one of fracture. One of his descriptions of a soldier with march foot gives the characteristic clinical picture. The soldier, after a long march, returned to camp complaining of a burning sensation in the midportion of his right foot. On the following morning, in spite of the fact that his foot had become swollen, he undertook an hour's march. The pain and swelling increased. Schulte mentioned that there was a distinct point of maximum tenderness over the proximal half of the second metatarsal bone with no tenderness over the first and fifth metatarsal bones. Twenty days later he was able to feel a firm lump in the area corresponding to the previous point of maximum tenderness, and the mass, by x-ray film, proved to be bony callus and a fracture. As to cause, Schulte mentioned that in jumping, running,

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5 Poulet, A. De l'osteoperiostite rhumatismale des metatarsiens, Arch de med et pharm mil **12** 245, 1888.

6 Martin, A. Inflammation periosto-arthritique du pied a la suite des marches, Arch de med et pharm mil **18** 336, 1891.

7 Busquet, P. De l'osteoperiostite rhumatismale des metatarsiens, Rev de chir Paris **17** 1065, 1897.

8 Stechow. Fussodem und Roentgenstrahlen, Deutsche mil-arztl Ztschr, **26** 465, 1897, Fussodem und Roentgenstrahlen, Internat Cong f Hyg & Demogr **8** 99, 1898.

9 Schulte. Die sogenannte Fussgeschwulst, Arch f klin Chir **55** 872 1897.

long marches or even walking while on nonactive duty the men would experience sudden attacks of pain and present typical march foot

Kirchner<sup>10</sup> reported a total of 82 cases, among which those involving the second and third metatarsal bones made up by far the largest percentage. He mentioned that the condition was common in civilian life, and his series included bakers, painters, laborers and soldiers. He further mentioned that each case was one of fracture and that trauma was the direct predisposing factor. The site of involvement was given as follows: second metatarsal bone, 40 cases, third, 31, fourth, 1, fifth, 1, second and third, 4, third and fourth, 5.

Thiele,<sup>11</sup> on the other hand, with a total of 33 cases, reported fractures in only 14 instances, but stated that periostitis was present in all, and that crepitation was elicited in 7 and abnormal mobility in 5. Periosteal proliferation could be detected in each case after a period of from eight to ten days.

Blecher<sup>12</sup> added reports of 78 cases to the literature. He was the first to make mention of recurrences in old fractures and reported 5 cases in which fresh fractures occurred in old healed ones a second, and in 2 cases a third, time. Definite fractures were observed in 30 cases, periostitis alone in 29 and no changes in 19. As to etiology, he felt that two factors were present: (1) an overburdening of soldiers, causing an undue strain on the metatarsal bones, and (2) a direct mechanical force causing the fracture.

Meiser<sup>13</sup> offered a point of some significance in stating that a fracture, although present in every typical case of march foot, could be demonstrated in only one third of the instances. Another was his theory of the etiology of march foot. He wrote that an elongated metatarsal bone is the probable cause of a weak foot, and that the weakness of the foot is proportional to the elongation of the metatarsal bone. (Dodd<sup>14</sup> in a more recent article considers the short first metatarsal bone as an outstanding factor in the cause of march foot.)

10 Kirchner, A. Ueber das Wesen der sogenannten Fussgeschwulst, Wiesbaden, J. F. Bergmann, 1898, *Die Fussgeschwulst*, *Deutsche mil-arztl. Ztschr.* **28** 79 1899. *Die Aetologie der indirekten Metatarsalfraktur*, *Arch. f. klin. Chir.* **77** 241 1905.

11 Thiele. Ueber Frakturen der Metatarsalknochen durch indirekte Gewalt (Fussgeschwulst), *Deutsche med. Wchnschr.* **25** 158, 1899, *Weiterer Beitrag nach der Ursache der sogenannten Fussgeschwulst*, *Deutsche mil-arztl. Ztschr.* **29** 129, 1900.

12 Blecher. Fussgeschwulst, Knochenbruch und Knochenhautentzündung, *Deutsche mil-arztl. Ztschr.* **31** 321 1902, *Entstehung der Fussgeschwulst*, *ibid.* **32** 3 1903.

13 Meiser. Die Brüche der Mittelfussknochen als Ursache der Fuss- oder Marschgeschwulst. *Fortschr. a. d. Geb. d. Röntgenstrahlen* **4** 105, 1901.

14 Dodd H. Pied Fource or March Foot, *Brit. J. Surg.* **21** 131 (July) 1933.



In direct contrast to Meiser, Thalwitzer<sup>15</sup> was a supporter of the theory that march foot is caused by periostitis and felt that fractures were present only when demonstrable

Eyles'<sup>16</sup> dissertation conforms more to the general than to some of the individual concepts of march foot. He offered one or more of the following points as positive findings in a typical case: (1) a definite area of callus, (2) a complete fracture without displacement, (3) a complete fracture with displacement, (4) an incomplete fracture and (5) periosteal thickening of the shaft of one or more bones.

In his experience the second and third metatarsal bones were most commonly involved and usually in the distal third.

Tobold<sup>17</sup> offered 1,500 cases with details of statistical value. Changes were found in 67.3 per cent of all cases. Fractures occurred in 49.7 per cent and periostitis in 11.9 per cent. Old fractures were found in 5.7 per cent and no fractures in 32.7 per cent of the cases. The metatarsal bones were the seat of involvement in the following percentages: second left, 13.2, second right, 10.8, third left 10.3, third right, 8.7.

Nion<sup>18</sup> also contributed statistics of value. In a series of 575 cases which he examined at the Roentgen Institute, he found changes in 330. The left foot was involved in 118 instances, the right, in 115 (including double changes). Fractures were seen in the metatarsal bones in 228 cases as follows: in the second metatarsal bone in 112, in the third in 98, in the fourth in 17, in the first in 1.

Runstrom<sup>19</sup> in an article on fresh subperiosteal hemorrhage in fractures of the metatarsal bones brought to light some interesting and important facts. To quote him verbatim:

My material at the Military Hospital comprises partly injuries after definite traumas—direct and indirect—and partly "marching injuries" without trauma.

I have divided the material into three groups according to the roentgenologic observations:

Group 1. Fourteen cases show a fracture or a fine fissure without dislocation and a thin spindle-shaped deposit. Two of these cases have occurred after a definite trauma and have been examined by means of the roentgen rays on the fourth and sixth days. Of the twelve remaining cases eight have been examined on the second to the fourth day and the rest on the sixth to the eighth day after the trauma.

15 Thalwitzer. Zur Aetiologie der Fussgeschwulst, Deutsche mil.-ärztl. Ztschr. **31** 435, 1902.

16 Eyles, F. Die Marschfraktur. München med. Wchnschr. **62** 1703, 1915.

17 Tobold. Zur Kasuistik der Mittelfussknochenbrüche, Deutsche mil.-ärztl. Ztschr. **32** 573, 1903.

18 Nion. Zur Statistik der Mittelfussknochenbrüche, Deutsche mil.-ärztl. Ztschr. **32** 200, 1903.

19 Runstrom, Gosta. Roentgen Picture of Fresh Subperiosteal Hemorrhages in Fractures of the Metatarsals, Acta radiol. **3** 42, 1924.

Group 2 Twelve cases show a thin spindle-shaped deposit but no absolutely provable fracture. Three of them have occurred after a definite trauma and have been examined on the first, fifth and seventh days. Of the "marching injuries" six have been examined on the third to the sixth day and the other ones on the seventh to the eighth day.

Group 3 Nineteen cases show fractures with distinct dislocation but no spindle-shaped deposit. Six of these have occurred after a definite trauma and have been examined on the first to the fifth day. Of the "marching injuries," twelve have been examined on the first to the fifth day, and one on the eighth day.

He concluded that a fracture is present in every instance and that the spindle-shaped deposit is merely subperiosteal hemorrhage, which cannot be present, and is not present, in group 3, in which dislocation of the fragments has occurred.

Jansen in 1916, and again in 1926, offered a more radical concept of the etiology of march foot. He felt that march foot is a complication of a subacute weakness of the foot and that the interosseus muscle plays an important rôle in bringing about bone changes. He emphasized the origin of the interossei, showing that they arise on the sides of the metatarsal shafts with the exception of the first bone and the lateral aspect of the fifth bone. He stated further that the spasm of the muscle bellies gives rise to an edema and hypertrophy of the muscle tissues and periosteum. At times an acute subperiosteal hemorrhage is formed. The periosteal changes are never on the outer border of the fifth or either border of the first metatarsal bones, only because the muscle does not have any of its origin in these areas. The bone, possessing no expansibility, becomes partly absorbed, brittle and more susceptible to fracture.

Dodd<sup>14</sup> questioned Jansen's theory of vascular disturbances and bone absorption and felt that the various changes as suggested by different authors—namely, tenosynovitis, spasm of muscles, arthritis, periostitis, synovitis—are merely manifestations of the weak foot. He emphasized the four points of Morton which are commonly seen in weak feet and offered a study of 14 cases which corroborated his theory.

Morton's points as given by Dodd are

- 1 Laxity of the joint between the internal cuneiform bones and between them and the scaphoid, resulting in hypermobility of the first metatarsal. This is shown by a distinct separation between the first and second cuneiforms, resembling a backward continuation of the first intermetatarsal space.
- 2 Shortness of the first metatarsal, this causing over-pronation of the foot, i. e., planus of the anterior part of the foot, as the head of the metatarsal is not long enough to reach the ground in the normal attitude.
- 3 Posteriorly located sesamoid bones at the head of the first metatarsal these representing its point of contact with the ground, and when they are posterior to the line of the head of the second metatarsal, they have practically the same effect as that of a short metatarsal, i. e., they prevent adequate weight-bearing by the first metatarsal.

4 Morton points out a further acquired physiological characteristic resulting from these defects, it is an enlargement of the shaft of the second metatarsal bone, especially in its transverse diameter, arising in response to the increased burden thrown on it by the incompetent first metatarsal

Dodd added a fifth factor in march foot, a thickening of the outer border of the first metatarsal bone, a finding in direct contrast to that of Jansen, who stated that periosteal proliferation is never present in this metatarsal bone Dodd, as did previous writers, stated that the



Fig 1—Left foot, anterior-posterior view, on Aug 29, 1934, showing a recent fracture at the base of the fifth metatarsal bone and an old fracture in the proximal fourth of the second metatarsal shaft (indicated by arrows) On the medial aspect of the middle third of the third metatarsal bone periosteal thickening may be seen The internal cuneiform bone presents slight lipping (Note that the heads and necks of the metatarsal bones are normal)

first metatarsal bone, being thicker and stronger than the remaining ones, is forced to bear the greater brunt of the body's weight, but that following a relaxation of ligaments the second, then the third and remaining metatarsal bones take on the strain but because of size are unable to sustain the force and fracture

PATHOLOGY OF MARCH FOOT

Dodd reported a case in which a Lisfranc amputation was performed because of a mistaken preoperative diagnosis of sarcoma. The case proved to be one of march foot. The pathologic specimen was reported to show rarefying osteitis of the metatarsal bone associated with chronic inflammatory periostitis.<sup>20</sup>

Strauss<sup>21</sup> reported a case of march foot that was preoperatively diagnosed as neoplasm and, because of this, the entire metatarsal bone

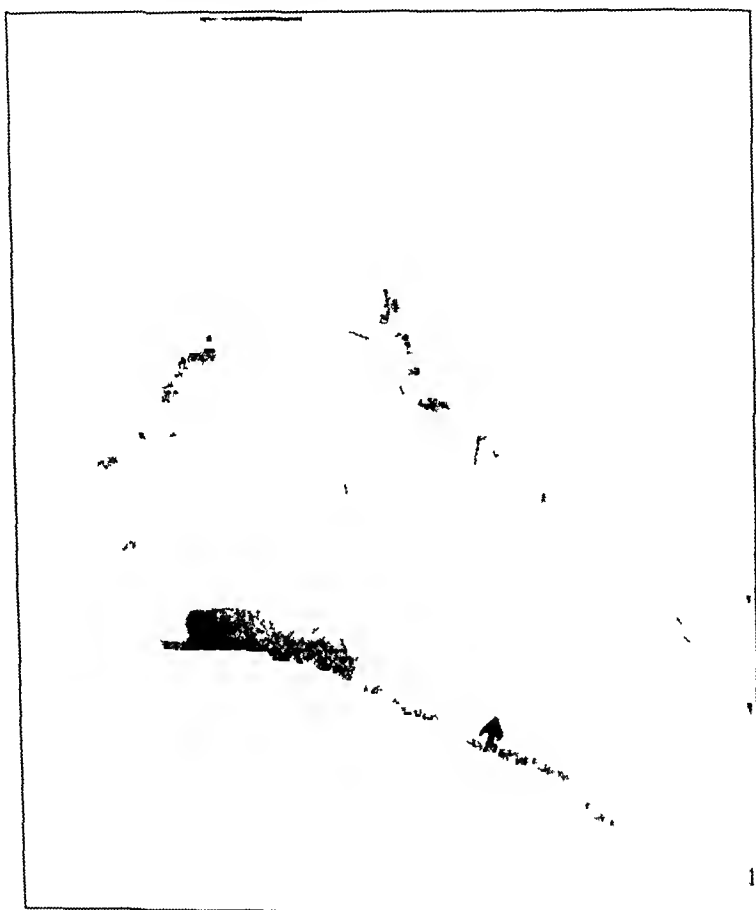


Fig 2—The same foot as in figure 1, lateral view

was removed. Pathologically the condition was found to be "a fracture of the shaft of the bone with incomplete repair, small hemorrhage and exuberant callus."

<sup>20</sup> Deutschlander (Ueber entzündliche Mittelfussgeschwulste, Arch f klin Chr **118** 530, 1921) considered march foot to be an inflammatory periostitis.

<sup>21</sup> Straus, F H. Marching Fractures of Metatarsal Bones with a Report of the Pathology, Surg, Gynec & Obst **54** 581 (March) 1932.

Each remaining author<sup>22</sup> has added to the long list of contributions to the knowledge of march foot, some by reports of cases, others by presentations of theory, and still others by articles of general discussion. Theories are numerous and probable causes many. Details were abstracted only when considered to be of some significance. Finer points, however, were very often lacking. At the close of this bibliographic abstract one important point should be emphasized, namely, that of the usual site of fracture or involvement in march foot. The proximal, middle and distal thirds were the only areas of bony changes suggestive of fracture, and these were usually in the middle and proximal thirds, never in the heads or bases of the bones. The tarsal bones, too, never showed any changes whereas the phalanges suggestively did in several instances<sup>23</sup>.

22 Bahr, F. Die Fussgeschwulst und ihre Beziehungen zum vorderen Frontalgewölbe, *Ztschr f Orthop Chir* **32** 310, 1913. Beely, F. Zur Mechanik des Stehens. Ueber die Bedeutung des Fussgewölbes, *Arch f klin Chir* **27** 457, 1882. Boisson, A., and Chapotot, E. Le pied force. Etude sur la nature et la pathogenie des lesions de l'avant-pied provoquées par la marche, *Arch de med et pharm mil* **33** 81, 1899. Goldman, S. E. March Foot with Fracture of Metatarsal Bone, *J Bone & Joint Surg* **10** 228 (April) 1928. Hamann, H. Ueber subcutane Fracturen der Metacarpal- und Metatarsalknochen mit besonderer Berücksichtigung des sogenannten militärischen Fussödems, *Dissert*, Greifswald, J. Abel, 1902. de Holstein, V. Les fractures des metatarsiens, provoquées par la marche, *Semaine med* **19** 187, 1899. Marey and Demeny. Locomotion humaine, mecanisme du saut, *Compt rend Acad d sc* **101** 489, 1885. Messerer, O. Ueber die Elasticitat und Festigkeit der menschlichen Knochen, Stuttgart, J. G. Cotta, 1880. von Meyer, G. H. Die Statik und Mechanik des menschlichen Knochengerüsts, Leipzig, Wilhelm Engelmann, 1873. Statik und Mechanik des menschlichen Fusses, Jena, Gustav Fischer, 1886. Momburg. Die Entstehungsurache der Fussgeschwulst, *Deutsche Ztschr f Chir* **73** 425, 1904. Monteith, W. B. R. Case of March Foot (Pied Force) with Signs of Old and Recent Injury, *Brit J Surg* **21** 708 (April) 1934. Muskat, Gustav. Die Brüche der Mittelfussknochen in ihrer Bedeutung für die Lehre von der Statik des Fusses, *Samml klin Vortr n F* October 1899, no 258 (*Chir*, no 76), p 1387. Nanoury, G. De la fracture du metatarse chez les jeunes soldats, *Rev d'orthop* **9** 349, 1898. Nasse and Borchardt, in von Bergmann, E., von Bruns, P., and Mikulicz, J. *Handbuch der praktischen Chirurgie*, ed 3, Stuttgart, Ferdinand Enke, 1907, p 947. Nimmer, H. De l'entorse metatarsienne chez les fantassins, *Arch de med et de pharm mil* **21** 61, 1893. Pirie, A. H. Marching Fractures, *Lancet* **2** 47 (July 14) 1917. Rittershausen. Zur Frage der Fussgeschwulst, *Deutsche mil-arztl Ztschr* **28** 18, 1899. Schipmann, G. Zur Kasuistik der Brüche der Metatarsalknochen, *Deutsche med Wchnschr* **25** 319, 1899. Sleswijk, R. Warum kommt die Fussgeschwulst beim Militär am meisten vor? *Deutsche mil-arztl Ztschr* **29** 552, 1900. Speed, J. S., and Blake, T. H. March Foot *J Bone & Joint Surg* **15** 372 (April) 1933. Tiedemann, E. Ueber die Häufigkeit und das Wesen der Fussgeschwulst, *Dissert*, Berlin, O. Francke, 1904. Trnka. Die subcutanen Frakturen der Metatarsalknochen, *Wien med Wchnschr* **49** 1879, 1899.

23 Dodd<sup>14</sup> interpreted phalangeal changes as those consisting of thickenings and fracture.

Retrospectively it may be stated that march foot is a complication of the "strained" foot, characterized usually by a sudden onset of pain and swelling on the dorsum and, to some degree, on the plantar aspect of the middle part and forepart of the foot. Clinically there is presented a tenderness over the shafts of one or more metatarsal bones and commonly at the junction of the middle and distal thirds of the second and

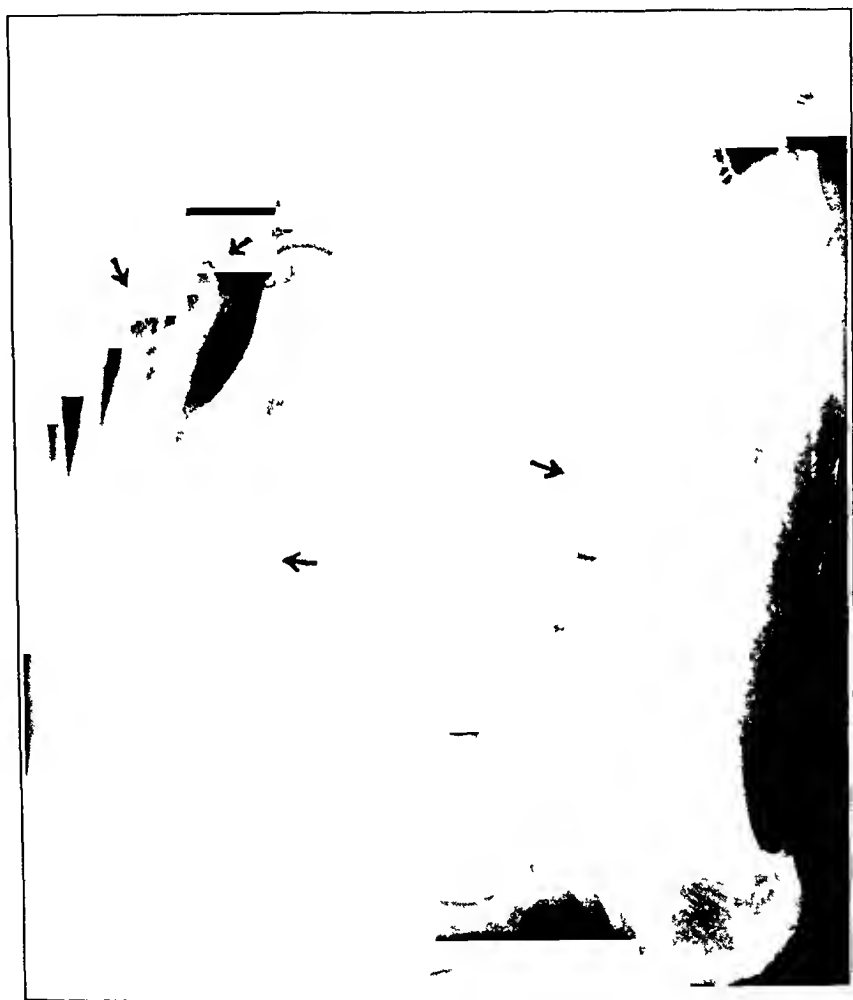


Fig 3—The anterior-posterior and lateral views of the left foot taken on Nov 30, 1934. There are fractures of the head of the second and neck of the third metatarsal bone (indicated by arrows). The internal cuneiform bone is fragmented in part (arrows). The fracture at the base of the fifth metatarsal bone is almost completely healed. (Note the unusual amount of callus in the neck of the third metatarsal bone.)

third metatarsal bones, rarely over the first or fifth. An x-ray picture, when taken immediately, frequently reveals no change but may present a fracture. Periostitis, with or without fracture, is often encountered at

an early date, but then, in all likelihood, the callus is of longer duration unless the early shadow, as Runstrom mentioned, is that of a subperiosteal hemorrhage. Periosteal changes are more commonly seen after ten days and fractures some weeks later. The latter, though, do not always make their appearance. Also, periosteal thickening on one or the other side of the shaft is often found associated with march foot.

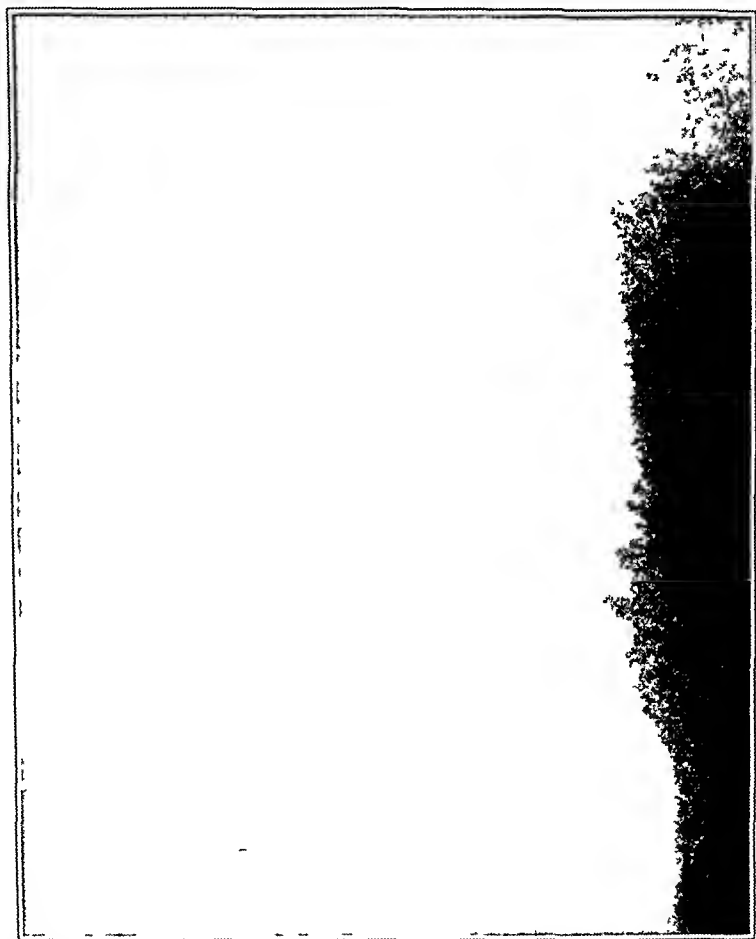


Fig 4—Magnification to show fragmentation of the internal cuneiform bone as indicated in figure 3

The etiology is still debatable. Periostitis and fracture are positive findings but can be considered only as the end-results of march foot.

The purpose of this paper is to describe changes in a case of march foot for which I can find no description in the literature. These changes, in addition to the usual findings, consisted of (1) fragmentation of the internal cuneiform bone, (2) fracture of the head of a metatarsal bone and (3) fracture of the base of a metatarsal bone.

## REPORT OF CASE

*History*—I A, a white man, 39 years of age, came to me complaining of pain and swelling of the left foot. On Sept 19, 1934, ten days prior to examination, he experienced a sudden attack of pain in the arch of his left foot. Because of this pain he found it difficult to walk but continued to do so until he found it almost impossible to "carry on." For a month or so prior to this acute attack he had experienced a tiredness which was more marked toward the end of the day or when he began to walk, especially after resting. There was a history of mild infection of the left big toe about the second week of August, but this cleared up rapidly, giving him no "trouble." He gave no history of a previous attack similar to this or of any involvement of other bones or joints. The remainder of his and of the family history was not relevant.

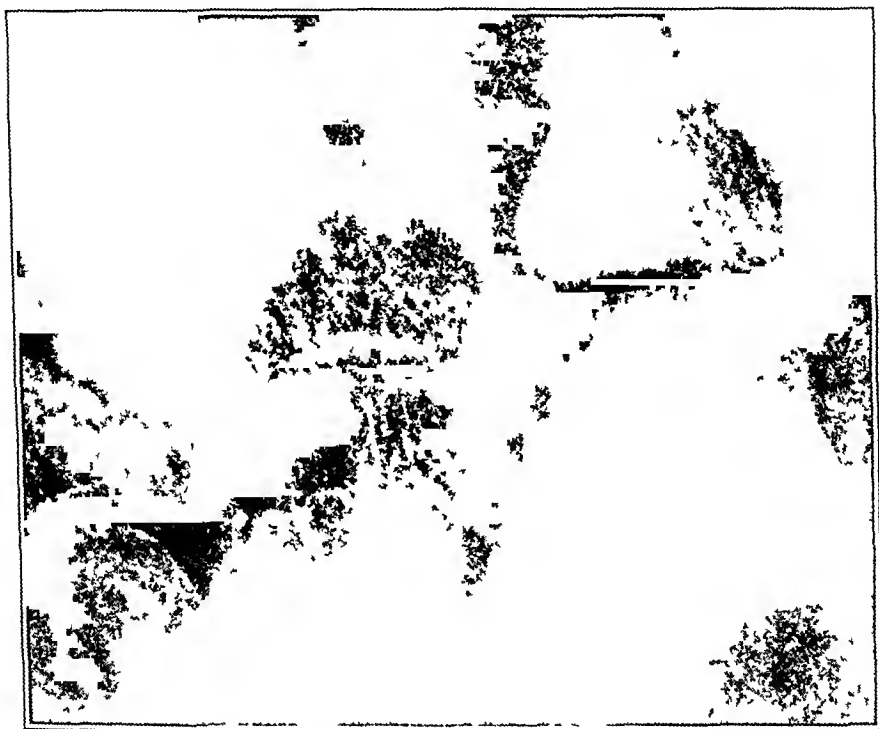


Fig 5—Magnification to show fractures of the head of the second and neck of the third metatarsal bone as indicated in figure 3

*Examination*—The left foot revealed a soft tissue swelling which extended from the toes to below the ankle joint. The edema pitted only slightly to firm touch. The toes and the heads of the metatarsal bones were not sensitive to pressure. Marked tenderness was present over the fifth metatarsal bone while the remaining shaft and the other metatarsal bones were free from symptoms. There was no abnormal mobility or crepitation. Motions of the toes were not restricted or painful. Inversion of the fore part of the foot was markedly limited and resulted in pain over the base of the fifth metatarsal bone. The heel was everted and adduction of the heel almost completely limited. Flexion and extension of the ankle joint were normal. The tendons of the anterior and posterior tibial muscles were tender at the points of their insertions. The tibial and fibular



shafts were not tender. The remaining examination of both lower extremities, including the right foot, the hips, the knee and right ankle joints, gave essentially negative results. Examination of the spine and upper extremities also gave negative results.

Roentgenographic examination of the left foot (figs 1 and 2) on September 29 showed a recent transverse fracture of the base of the fifth metatarsal bone with comminution of the proximal fragment. There was an old healed fracture in the proximal fourth of the second metatarsal shaft with some periosteal proliferation.

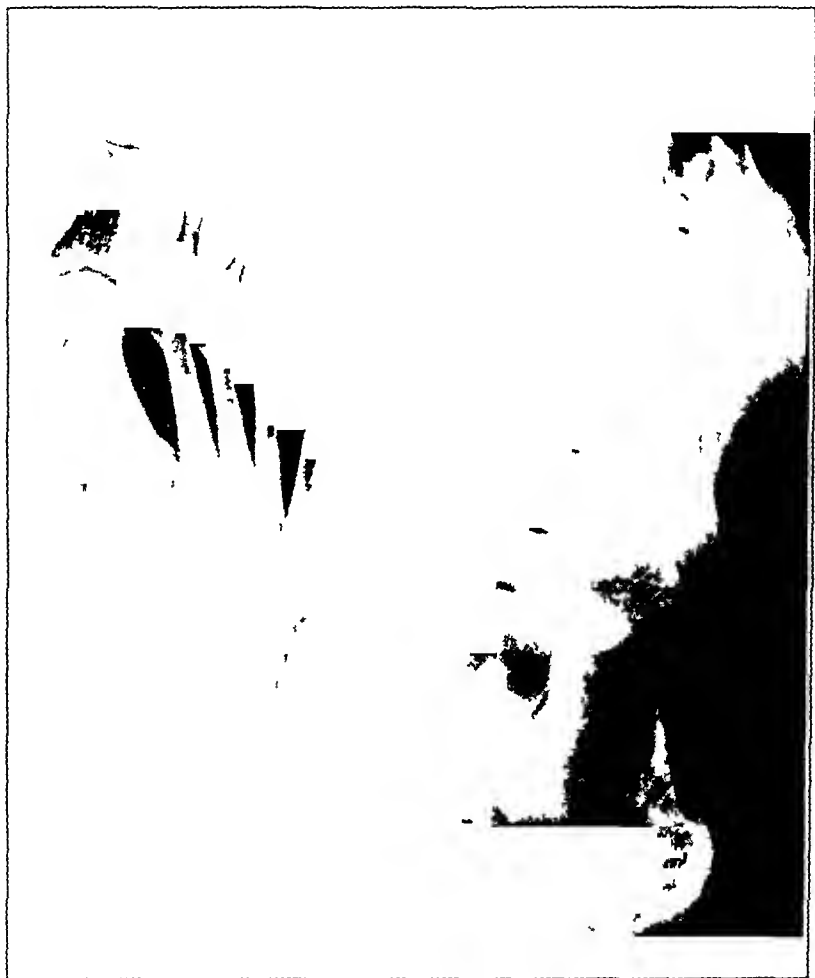


Fig 6—Right foot on Nov 30, 1934. The medial aspect of the middle third of the third metatarsal bone presents some periosteal thickening.

A localized area of periostitis was seen on the mesial side of the middle third of the third metatarsal bone. There was some sharpness of part of the internal cuneiform bone. A small gouged out area was present on the lateral aspect of the first metatarsal head and a similar area, on the posterior articular border of the tibia. A spur projected from the inferior border of the os calcis.

The observations on the blood were as follows: hemoglobin, 14.6 Gm, or 86 per cent, red blood cells, 5,080,000, white blood cells, 7,850, polymorphonuclears,

60 per cent, small lymphocytes, 22 per cent, large lymphocytes, 4 per cent, mononuclears, 9 per cent, eosinophils, 1 per cent, bleeding time, eight and one-half minutes, coagulation time, five and one-half minutes, blood calcium, 10.4 mg, blood phosphorus, 2.6 mg, Wassermann and Kolmer reactions, negative

*Diagnosis*—The diagnosis was march foot

*Treatment and Clinical Course*—The foot and ankle were immobilized with adhesive strapping, and bearing of weight was not permitted. This treatment was later followed by baking and by gentle and then more vigorous massage, aiming particularly at the spasticity of the muscles. The condition improved

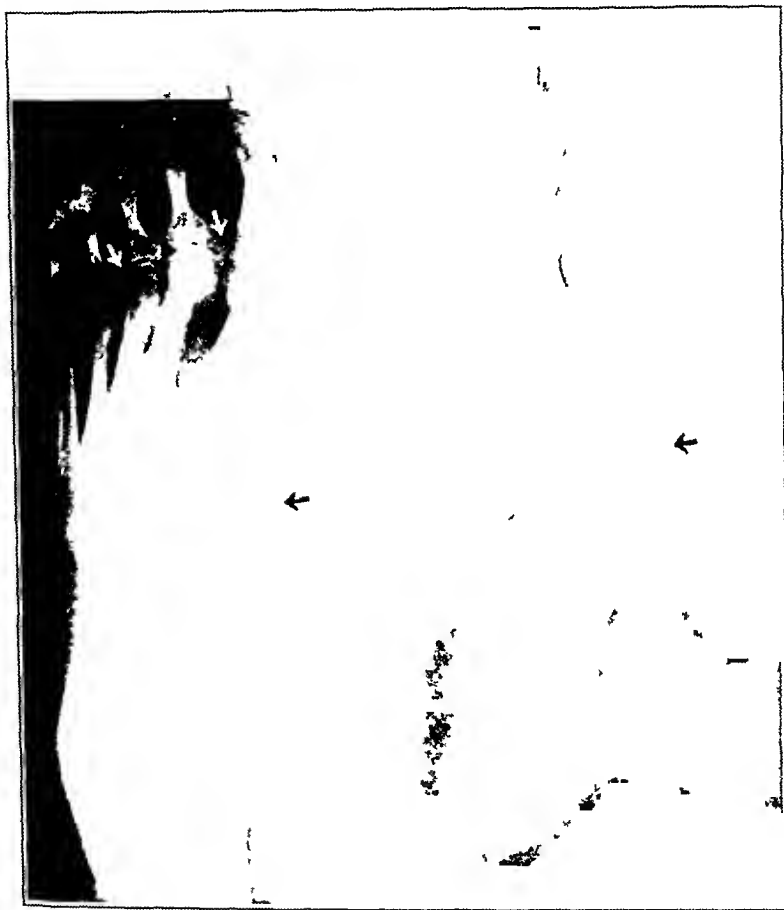


Fig 7—Left foot, anterior-posterior and lateral views, on Dec 27, 1934. There is further evidence of fracture of the head of the second metatarsal bone with a suggestive V formation at the neck. The base of the fifth metatarsal bone and the neck of the third metatarsal bone show further evidence of healing.

gradually under treatment, and the patient began to walk with the aid of arch supports. On November 30, he complained of some discomfort in the fore part of the foot. Examination revealed distinct areas of thickening with some tenderness of the second and third metatarsal heads, immediately behind the metatarsophalangeal joints. There was no gross swelling of the toes or foot. Abduction of the heel was now only slightly limited, but inversion of the fore part of the foot was markedly limited, while motions of the toes were free. X-ray films

taken of both feet (figs 3 to 6) revealed a healing fracture at the neck of the third metatarsal bone of the left foot with some medial displacement of the distal fragment and exuberant formation of callus. Another startling finding was the fragmentation of the internal cuneiform bone with some irregularity of part of the articular surface of the scaphoid. The distal half of the second metatarsal bone showed periosteal proliferation and a fracture of the head beginning in the lateral aspect, running transversely across immediately distal

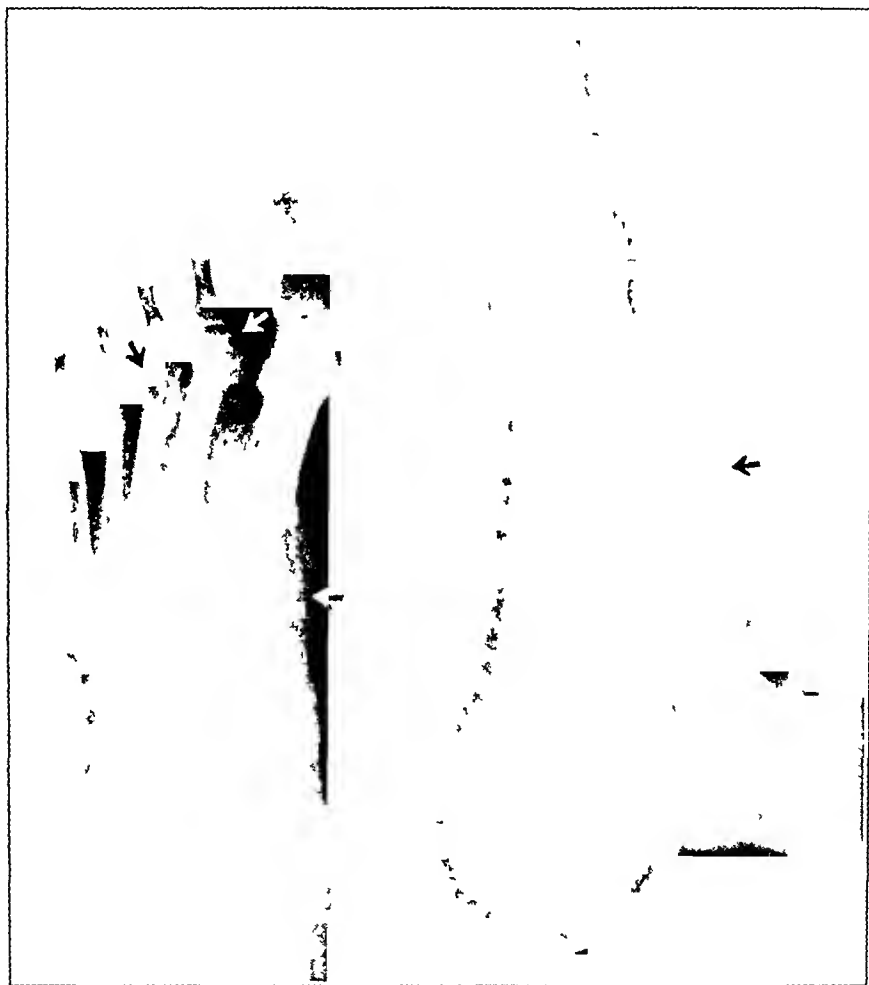


Fig 8—Left foot, anterior-posterior and lateral views, on Jan 30, 1935. There is further evidence of healing at the base of the fifth metatarsal bone, neck of the third and head of the second. The internal cuneiform bone shows greater evidence of fragmentation, and several fragments of bone can be more clearly seen on the lateral view.

to the articular surface and passing into the neck. The old fracture at the base of the fifth metatarsal bone showed healing and a faint line of periosteal proliferation. The head of the fourth metatarsal bone showed a suspicious line of fracture. The right foot showed a slight thickening on the medial aspect of the middle third of the third metatarsal shaft.

The metatarsal arch was raised, and the patient showed further improvement. Physical therapy was continued.

On December 27, examination of the left foot showed further improvement. The tenderness over the heads of the second and third metatarsal bone had disappeared, adduction of the heel was fairly free, but pronation of the fore part of the foot was still limited. An x-ray film was again taken of the left foot (fig 7). There was evidence of further healing at the base of the fifth and neck of the third metatarsal bone. The head of the second metatarsal bone showed further evidence of a fracture, and there was also a suspicious V formation at the neck.

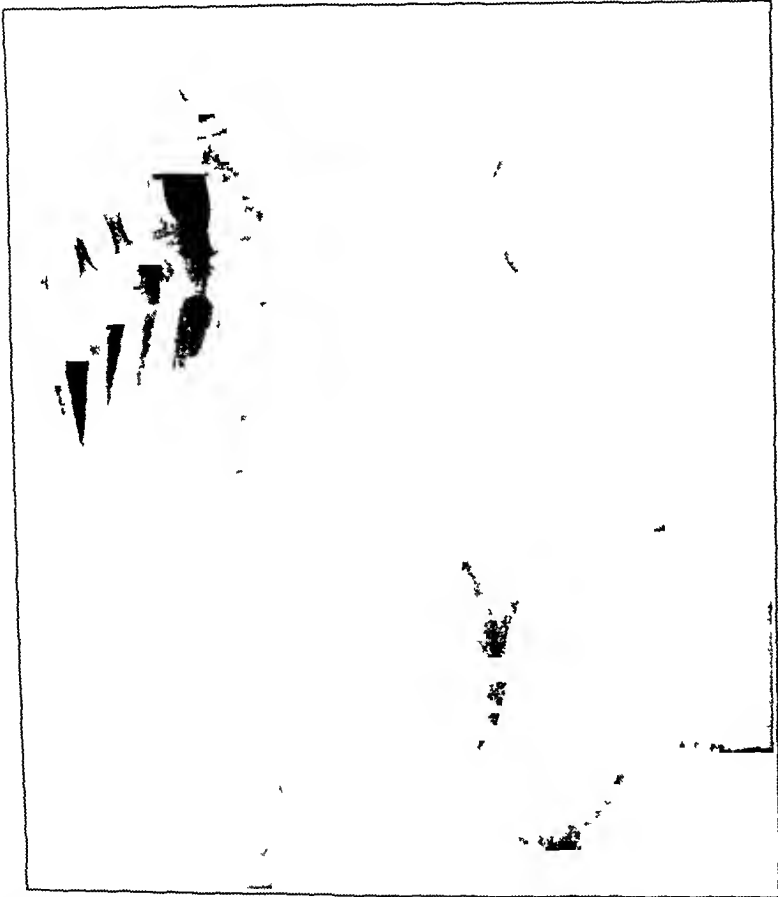


Fig 9—Right foot, anterior-posterior and lateral views, on Jan 30, 1935. There are no changes over those found at the first examination.

The patient was reexamined on Jan 30, 1935. He was free from pain and no longer complained of tiredness. Adduction of the heel and pronation of the fore part of the foot were free. There were no areas of tenderness. Roentgen examination of the left foot (fig 8) showed further healing at the base of the fifth, neck of the third and head of the second metatarsal bone. The internal cuneiform bone gave greater evidence of fragmentation, and several fragments of bone could be more clearly seen on the lateral view. The x-ray film of the right foot (fig 9) offered no changes over those observed at the previous examinations.

The changes presented by this unusual case emphasize the possibility that fragility of bone may play an important role in the fractures of march foot. It is not likely that similar changes had not occurred in the thousands of cases that preceded this one, in all probability some of the earlier observers overlooked them. Of still further interest is the fact that these changes partly substantiate the etiologic theories of some and deny those of others, and one may conclude that more serious thought and consideration should be given to the possibility of calcium disturbances in the bone proper.

#### SUMMARY

A case of march foot with several undescribed bone changes is presented. These changes were (1) fragmentation of the internal cuneiform bone, (2) a fracture of the head of the second metatarsal bone and (3) a fracture of the base of the fifth metatarsal bone.

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# ACUTE APPENDICITIS AND ASSOCIATED LESIONS

## SOME OBSERVATIONS ON THE MORTALITY

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In the study of acute appendicitis for the eighteen year period between Jan 1, 1916 and Jan 1, 1934, at the Presbyterian Hospital in New York, it was discovered that a considerable number of the case records were classified under improper subgroups. In order to procure accurate information on the total mortality rate, as well as that of the individual subgroups, it was necessary to examine the history on every case record which had been filed under the following classifications: acute appendicitis, acute appendicitis with acute local peritonitis, acute appendicitis with peritoneal abscess, acute appendicitis with acute diffuse peritonitis and acute appendicitis with progressive fibrinopurulent peritonitis. Therefore, by careful search of these records, it was possible to present the facts which constitute this paper.

Numerous discrepancies were found between the final diagnosis listed on the record cards and the operator's description of the pathologic process or the final note. Such a discrepancy was often strengthened by the clinical symptoms and signs as noted by the house surgeon or by the attending surgeon. For instance, there were many charts on which a final diagnosis of acute appendicitis was recorded which obviously belonged to the group filed under acute appendicitis with acute local peritonitis. There were numerous case records filed under acute appendicitis with acute local peritonitis which on careful examination indicated that they should have been placed elsewhere: either under acute appendicitis or acute appendicitis with acute diffuse peritonitis or even under acute appendicitis with peritoneal abscess. This same situation obtained in the other groups studied. Sometimes two associated phases were found in one chart. This was particularly true of those filed under acute appendicitis with peritoneal abscess, in this group acute diffuse peritonitis was also recorded on seventy-seven charts, some of these were merely filed under acute diffuse peritonitis, while several were found only under the caption of peritoneal abscess, and the remainder were properly placed under both headings. Similarly, there were 2 instances of appendiceal abscess and progressive fibrinopurulent peritonitis which were listed only under one diagnosis. In this connection, when more than one associated lesion existed, it must be emphasized

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From the First Surgical Service of the Presbyterian Hospital

that such cases were assigned under each of the two groups to which they belonged, and if the patient died the fatality was recorded under each of these groups in the computation of the mortality rate for each separate group (chiefly in tables 1, 4, 7, 10 and 13) but in determining the total mortality rate for all the groups (table 15) these same cases in which more than one lesion was present were counted only as 1 case, and, if the patient died, only 1 death was recorded. This accounts for the fact that the sum of the individual series (tables 1, 4, 7, 10 and 13) would be greater than the total as given in table 15. Mention must also be made of those cases in which there were preoperative signs and symptoms and a gross operative pathologic process of acute appendicitis, yet in which the microscopic diagnosis failed to reveal an acute inflammatory process. The records in these cases were nevertheless filed under acute appendicitis provided the attending surgeon in his final note still considered the case as one of acute appendicitis. Several cases were found in which the history and physical signs and the appearance of the appendix did not warrant the diagnosis of an acute process, and these were excluded except in 2 or 3 instances in which the microscopic diagnosis was acute appendicitis despite the clinical evidence to the contrary.

The reader will note that acute appendicitis together with its associated lesions has been placed under five main groups (tables 1 to 14). They do not necessarily represent consecutive stages of the same disease process. Often they skip the stage of peritoneal abscess (tables 7 and 8) and proceed from one of local to one of diffuse (or spreading) peritonitis and then perhaps finally to fibrinopurulent peritonitis. There are a number of instances in which peritoneal abscess with acute diffuse peritonitis, and even with acute fibrinopurulent peritonitis, has been described at operation, although here it is likely that the abscess was present before the diffuse or fibrinopurulent peritonitis developed.

It must be realized that the five groups into which these cases have been divided are classified possibly for the purpose of convenience and study rather than as actual separate clinical entities, although in the great majority of instances the latter also probably obtains. Yet there must be many cases in which it would be extremely difficult to determine the exact category. Add to this the individual interpretation and conception of the disease process on the part of a score or more surgeons and the reader will quickly challenge the accuracy of tables 1 to 14. There is no satisfactory answer to this except to state that all questionable cases were discussed and reviewed with the attending surgeon in charge, and his decision (to which group they should belong) was considered as final. Table 15, however, represents the total number of cases of acute appendicitis of all types, together with the actual number of deaths, therefore, the figures in this table can be considered as accurate.

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## GROUP 1 ACUTE APPENDICITIS

*Definition*—Acute appendicitis is an acute inflammatory process confined almost entirely to the appendix, in whole or in part. The organ is edematous and sometimes turgid and distended. Its serosa has lost its luster, and the serosal vessels are often dilated. There may be some deposition of fibrin and even beginning discoloration suggesting an early stage of gangrene. The meso-appendix often presents edema, dilatation of the blood vessels and friability. The cecum, adjacent intestinal coils, mesentery, retroperitoneal tissues and parietal and visceral peritoneum show little or no inflammatory reaction. There is usually no exudate.

TABLE 1—*Annual Mortality Rates in Cases of Simple Acute Appendicitis at the Presbyterian Hospital*

Years	Number of Cases	Number of Deaths	Mortality, per Cent
1916	49	1	2.0
1917	44	0	0
1918	60	0	0
1919	43	0	0
1920	60	1 (0)*	1.66
1921	53	0	0
1922	54	1	1.85
1923	61	0	0
1924	54	1	1.85
1925	50	0	0
1926	56	0	0
1927	69	0	0
1928	74	1	1.35
1929	93	1	1.07
1930	87	0	0
1931	91	1 (0)*	1.09
1932	65	0	0
1933	112	0	0
Total	1,175 (1,173)*	7 (5)*	0.59 (0.42)*

\* See analysis of deaths, page 67.

*Mortality Rate*—In table 1 are listed the number of cases which conform to the definition just stated, with the number of deaths and the mortality rate. It is interesting to study the progressive five year average mortality rate for comparison, because it tends to lessen the fluctuation factor of each individual year (table 2). This is more striking in comparing the graphs in charts 1 and 2. The line in chart 2 is surprisingly level, but one notes immediately an upward progression from 0.34 per cent in the period from 1923 to 1927 to 0.73 per cent in the interval from 1928 to 1932. The latest five year average (1929-1933) has diminished markedly and is the third lowest in the series. Therefore, although the mortality rate at the Presbyterian Hospital is no higher than that of the earlier years, still there has been a slight but definite increase since 1925 up to the latest five year period. The total death rate for all the cases in this group from 1916 to 1933 inclusive, is 0.59 per cent.



*Comparative Study*—Some figures from other clinics and hospitals will be interesting for comparison, and these are shown in table 3. It will be noted that the mortality rates vary considerably. Probably the most interesting figure is that of Bauer, who has made a most careful and scholarly study of cases of acute appendicitis covering a period of twenty-seven years. It did not seem fair to quote mortality rates from a personal series (such as Guerry<sup>1</sup>) or from a small, limited group of highly trained surgeons (Finney's<sup>2</sup> series, for instance), because the

TABLE 2—*Progressive Five Year Average Mortality Rates in Cases of Simple Acute Appendicitis at the Presbyterian Hospital*

Years	Number of Cases	Number of Deaths	Mortality, per Cent
1916-1920	256	2	0.78
1917-1921	260	1	0.38
1918-1922	270	2	0.74
1919-1923	271	2	0.73
1920-1924	282	3	1.06
1921-1925	272	2	0.73
1922-1926	275	2	0.72
1923-1927	290	1	0.34
1924-1928	303	2	0.66
1925-1929	342	2	0.58
1926-1930	379	2	0.52
1927-1931	414	3	0.72
1928-1932	410	3	0.73
1929-1933	448	2	0.44

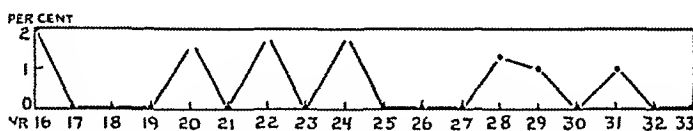


Chart 1—Graph showing the annual death rate from 1916 to 1933, inclusive, in 1,175 cases of simple acute appendicitis. The total number of deaths was 7, the mortality rate, 0.59 per cent.

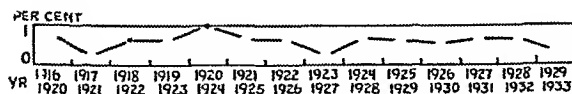


Chart 2—Graph for comparison with that in chart 1, showing the progressive five year average death rate from 1916 to 1933, inclusive, in the same group of cases of simple acute appendicitis.

present report represents the results of a large hospital staff in which there have been at least twenty-five attending surgeons during the period under study. Many reports were found in the literature, but they are not shown in table 3 because the period of time was too short or because the series was too small. This fact also obtains in comparing the mortality

1 Guerry, Le G. *Tr Am S A* 44 136, 1926.

2 Finney, J. M. T., Jr. *Surg, Gynec & Obst* 56 360 (Feb) 1933.

rates in groups 2 to 6 at the Presbyterian Hospital. Another difficult feature in endeavoring to make comparisons is that each hospital or locality has its own classification of acute appendicitis and its associated lesions. Consequently, the reader must appreciate a real factor of error in studying these charts. However, I have attempted to cite only those series which might seem to agree with the classification used in this paper. In passing, it is interesting to note that two authors (Dixon<sup>3</sup> and Stoney,<sup>4</sup> both personal series) do not have a single death in their group of cases of simple acute appendicitis.

*Analysis of Deaths*—A careful study of the 7 fatal cases in this group revealed 2 in which the data furnish considerable doubt as to the validity of the cause of

TABLE 3—*Mortality Rates in Series of Cases of Acute Appendicitis Reported in the Literature*

Year of Publication	Author	Place	Number of Cases	Period Studied	Mortality, per Cent
1925	Adams <sup>7</sup>	London Hospital	633	1919-1923	0.9
1925	Love <sup>8</sup>	St. Thomas' Hospital	348	1919-1923	0.8
1927	Colp <sup>9</sup>	Mount Sinai Hospital, New York	842	1916-1926	0.95
1928	Quain and Waldschmidt <sup>10</sup>	Bismarck, N. D.	551	1919-1927	0.36
1931	McDonald, Minnesota Med 14: 212, 1931	St. Marys and St. Lukes Hospital, Duluth, Minn.	944	1925-1930	0.74
1933	Bauer <sup>11</sup>	General Hospital, Malmo, Sweden	3,750	1903-1930	0.7
1933	Walker <sup>12</sup>	Boston City Hospital	1,174	1927-1930	1.5
1933	Coller and McRae, J. Michigan M. Soc. 30: 319, 1931	University Hospital, Ann Arbor, Mich.	233	1925-1930	0.43
1934	Keyes, Ann. Surg. 99: 47, 1934	Barnes and St. Louis Children's Hospitals	345	1915-1932	2.32
1934	Quain, Arch. Surg. 78: 28, 1934	Bismarck, N. D.	637	Sept. 1927 to Oct. 1932	0.31

death. One patient was a 6 year old child who was admitted to the hospital with a diagnosis of intussusception. The diagnosis was verified at operation, and the appendix was found to be included in the ileocecal intussusception. After reduction was accomplished, the operator examined the appendix and thought it appeared acutely inflamed. It was therefore removed. The report from the surgical pathology laboratory was chronic appendicitis. The patient lived only ten hours after operation. It is possible that the appendix was simply congested by reason of its inclusion in the intussusception instead of being primarily acutely inflamed.

The second doubtful case was that of a 27 year old man who was admitted to the hospital because of pneumonia (type I) and a failing heart from chronic cardiac valvular disease. The abdomen was slightly distended, and no tenderness or spasm was present. The patient died five hours later. Autopsy revealed obvious pneumonia, edema of the lungs and cardiac hypertrophy as well as mitral and aortic stenosis. The abdominal cavity was clean, and the peritoneum was smooth, pale

<sup>3</sup> Dixon, C. F. Proc. Staff Meet., Mayo Clin. 7: 323 (June 1) 1932.  
<sup>4</sup> Stoney, R. A. Irish J. M. Sc. 2: 645 (Nov.) 1932.

## ARCHIVES OF SURGERY

and glistening. The appendix appeared normal in its proximal two-thirds, but the distal third was slightly distended. Here the serosa was distinctly congested. Section of this portion of the appendix disclosed a thickened edematous wall, and the lumen contained a few drops of pus. The microscopic picture indicated an acute inflammatory process. One may almost certainly accept the pulmonary and cardiac pathologic processes as the primary causes of death.

Two fatalities were due to pulmonary embolism, they occurred on the fifth and on the sixth day after operation. The first fatality was that of a man aged 29, who had a smooth postoperative course following the removal of an acutely inflamed retrocecal appendix. The other patient, an obese man of 52, suffered from marked postoperative distention. The operation lasted eighty minutes because of great difficulty in removing the appendix.

Another patient, 13 years of age, was admitted to the hospital with the diagnosis of tuberculous peritonitis and chronic ileus. A few days later rather severe pain developed in the right lower quadrant of the abdomen. Operation disclosed an acutely inflamed appendix and a complete lack of evidence of tuberculous peritonitis. Three days later there were signs of atelectasis of the left lung, together with bronchopneumonia. On the eleventh day acute ileus occurred. Cecostomy was performed because a mass presumably inflammatory, was discovered in the transverse colon. Following this episode, a chronic cough developed with signs of bronchopneumonia over the lower lobe of the left lung. Because of the persistence of the cough and pulmonary signs, it was felt that the process might be tuberculous, but repeated examination of the sputum did not reveal any tubercle bacilli. On the fortieth day severe stomatitis set in and spread rapidly to all parts of the oral cavity, producing extensive unclean ulcers. The patient became rapidly worse and died on the fiftieth day.

The remaining 2 cases are interesting in that death might have been prevented by the use of spinal anesthesia or avertin, or even of local anesthesia. The patient in the first case was a man of 38 who had a cold and sore throat at the time of admission. Ethylene was poorly taken, so it was decided to give ether by the open method. The operation was long and difficult because of nonrotation of the cecum together with a retrocecal position of the appendix. Bronchopneumonia (type IV) developed on the fourth day. The severe coughing provoked disruption of the wound on the eighth day, and it was immediately repaired. Death followed in twenty-four hours. The other patient was a very obese man of 52 years. The operation lasted one and a half hours because of difficulty in removing a high retrocecal appendix. Ethylene-ether anesthesia was given. The postoperative course was stormy because of progressive distention and also bronchopneumonia in the lower lobe of the right lung. Jejunostomy was performed on the fourth day, at which time there was no evidence of peritonitis. The patient died twelve hours later.

It is interesting that all 7 deaths occurred in males. If one invalidates the first 2 deaths as being primarily nonappendical in origin, then the total mortality rate for simple acute appendicitis would be 0.42 per cent instead of 0.59 per cent (table 1\*).

#### GROUP 2 ACUTE APPENDICITIS WITH ACUTE LOCAL PERITONITIS

*Definition*—The condition is an acute inflammatory process which is not confined to the appendix alone but involves the viscera in the close vicinity as well as the adjacent parietal and visceral peritoneum. In

addition to the pathologic process noted in the previous group, there may be considerable deposition of fibrin on the appendix. The latter may show more advanced signs of gangrene. There is usually no gross perforation. The cecum about the base of the appendix may be edematous, thickened and congested. The omentum which is edematous and congested, is sometimes found partly or wholly enveloping the appendix, perhaps with the formation of a few delicate adhesions. The adjacent intestinal coils may be slightly dilated and sometimes there are congestion and loss of luster of the serosal surface. This same appearance may be found on the mesentery of the terminal portion of the ileum.

TABLE 4—*Annual Mortality Rates in Cases of Acute Appendicitis with Acute Local Peritonitis at the Presbyterian Hospital*

Year	Number of Cases	Number of Deaths	Mortality per Cent
1916	29	0	0
1917	29	0	0
1918	25	2	8.0
1919	29	0	0
1920	30	1	3.3
1921	41	2 (1)*	4.87
1922	35	1	2.85
1923	35	1	2.85
1924	32	1	3.12
1925	34	0	0
1926	45	2 (1)*	4.44
1927	33	0	0
1928	34	1	2.94
1929	40	0	0
1930	20	1	5.0
1931	22	0	0
1932	77	0	0
1933	40	0	0
Total	630 (628)*	12 (10)*	1.90 (1.59)*

\* See analysis of deaths page 72

Some peritoneal exudate is almost always present. It may be confined to the right lower quadrant or perhaps only to the iliac fossa, on the other hand, there may be a small collection in the pelvis in addition. This exudate may be clear, pale and odorless, but it is often turbid and grayish yellow and possibly slightly odorous. Sometimes it appears as a brownish seropurulent fluid but it is rarely bloody, frankly purulent or foul-smelling. The parietal peritoneum overlying the involved area may be edematous and injected. Briefly, the process is more extensive than that of the previous group, yet it tends to remain relatively confined to a limited area of the peritoneal cavity.

*Mortality Rate*—Table 4 together with charts 3 and 4, gives the facts concerning the annual death rate and the five year average. Here again chart 3 shows a fluctuating curve. In chart 4 one is

impressed by a definite, general decline, which reaches its lowest point in the last five year period. There are a few rises interspersed along the curve, the most serious being during the period from 1918 to 1922, inclusive. The mortality rate in the group of acute appendicitis with acute local peritonitis is definitely decreasing up to the present time, perhaps it will continue to do so. The total death rate in this group is 1.9 per cent, but the rate for the most recent five year period is only 0.5 per cent.

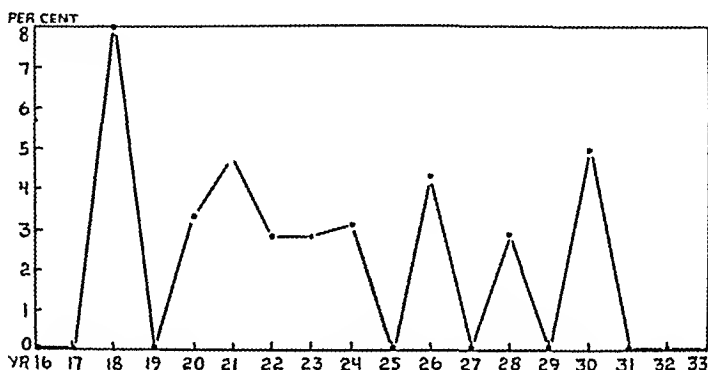


Chart 3—Graph showing the annual death rate from 1916 to 1933, inclusive, in 630 cases of acute appendicitis with acute local peritonitis. The total number of deaths was 12, the mortality rate, 1.9 per cent.

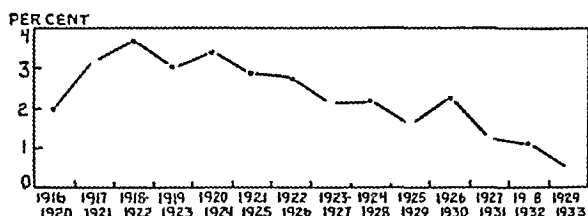


Chart 4—Graph for comparison with that in chart 3 showing the progressive five year average death rate from 1916 to 1933, inclusive, in the same group of cases of acute appendicitis with acute local peritonitis.

*Comparative Study*—Examination of mortality reports from other clinics indicates that the death rate at the Presbyterian Hospital compares rather favorably with them. This is shown in table 6. Even the mortality rates in the personal series of Ashhurst<sup>5</sup> (4.5 per cent), Stoney<sup>4</sup> (2.2 per cent) and Hawe<sup>6</sup> (2.8 per cent) are slightly higher.

*Analysis of Deaths*—There were 12 deaths in this group of cases. In 2 the cause of death seems doubtful from the standpoint of acute appendicitis with acute

5 Ashhurst, A. P. C. *Ann Surg* 85:89 (Jan) 1927.

6 Hawe, P. *Liverpool Med-Chir J* (pt 1) 41:89, 1933.

local peritonitis. The first case was that of a 9 year old boy who was observed for four days after admission to the hospital because of extremely confusing signs, which seemed to point to meningitis. Abdominal examination failed to reveal any signs of acute peritoneal irritation. The boy was extremely irritable, his neck was slightly stiff, there was a questionable Kernig sign, but examination of the fundi and spinal fluid gave negative results. The white blood cells numbered 31,000, with 84 per cent polymorphonuclears, and a culture of the blood showed a growth of the hemolytic streptococcus. The temperature remained around 104 F. Finally, on the fourth day, signs of tenderness in the lower portion of the abdomen and slight involuntary muscle spasm developed. At operation the picture was one of acute mesenteric adenitis, there was a small amount of clear, odorless, sticky exudate. The appendix was retrocecal and did not appear to be inflamed. However, the surgical pathology laboratory reported a diagnosis of acute appendicitis. The patient died two days later, having lapsed into coma and acidosis. Permission for autopsy was not obtained.

The second doubtful case was that of a girl, aged 14 years, who was admitted to the hospital with a diagnosis of acute appendicitis. There was an elevated blood count and an increase in the number of polymorphonuclears. At operation, acute local peritonitis was discovered. The appendix was laterocecal, and the distal two thirds was gangrenous, it was decided to use a drain. The postoperative course was uneventful, and the patient was discharged on the fifteenth day with instructions to visit the surgical clinic because the wound had not quite healed. During the following five weeks the wound showed no tendency to heal, in fact, it became slightly deeper. It had an unclean appearance, with unhealthy, grayish granulations and a thin, seropurulent discharge. During the fifth week the girl felt weak and feverish and lost her appetite. When the next dressing was applied, her general appearance was found to be distinctly poor, the temperature was 100 F and, to the astonishment of the examiner, the white blood count was 15,000, with 88 per cent large lymphocytes and immature forms. Further investigation showed an enlarged spleen and liver, but there was little or no general adenopathy. The patient was readmitted to the hospital and observed for two days, and then, because of increasing pain in the right lower quadrant, together with rising temperature and an increasing white cell count, the wound was explored, but no foreign body or residual abscess was found. A culture of the wound tract showed a growth of hemolytic streptococcus. The patient became rapidly worse, a blood culture on the third day after operation was positive for the hemolytic streptococcus. Subsequent blood counts revealed rapidly developing aleukemic leukemia. Petechiae soon appeared, and just before death there was severe ulcerative stomatitis. The final report of the autopsy and microscopic examination was acute lymphatic leukemia and hemolytic streptococcal bacteremia. It was the pathologist's belief that the leukemia probably existed before the episode of acute appendicitis took place.

If the cause of death in these 2 cases can be assigned to sources other than acute appendicitis with acute local peritonitis, the total mortality rate would be 1.59 per cent (table 4\*).

The remaining 10 deaths deserve some discussion. Six of the patients were aged 20 years or less. All 10 gave a relatively short history (with 1 exception). A recent acute infection of the respiratory tract had occurred in 2, and 1 patient gave a history of several attacks of pneumonia. As 1 man was an extensive user of alcohol, it was necessary to administer ether by the open method. Four patients received nitrous oxide and ether, and another was given chloroform and ether. Ethylene was used once. The anesthesia in the remaining case was started with

nitrous oxide and ether but, because of cyanosis and spasm, ether by the open method was substituted. The position of the appendix varied considerably. More significant are the following facts. Removal of the appendix was extremely difficult and the operation was considerably prolonged in 3 cases (either by reason of the obesity of the patient, poor relaxation and response to the anesthetic, or because of the position of the appendix itself involving serious technical difficulties), the large bowel was accidentally opened in 1 case, and in 2 the appendix ruptured during the process of removing it. These are all serious accidents, and they fur-

TABLE 5—*Progressive Five Year Average Mortality Rates in Cases of Acute Appendicitis with Acute Local Peritonitis at the Presbyterian Hospital*

Years	Number of Cases	Number of Deaths	Mortality, per Cent
1916-1920	142	3	2.11
1917-1921	154	5	3.24
1918-1922	160	6	3.75
1919-1923	170	5	2.94
1920-1924	173	6	3.46
1921-1925	177	5	2.82
1922-1926	181	5	2.76
1923-1927	179	4	2.23
1924-1928	178	4	2.24
1925-1929	186	3	1.60
1926-1930	172	4	2.32
1927-1931	149	2	1.34
1928-1932	193	2	1.03
1929-1933	199	1	0.50

TABLE 6—*Mortality Rates in Series of Cases of Acute Appendicitis with Local Peritonitis Reported in the Literature*

Year of Publication	Author	Place	Number of Cases	Period Studied	Mortality, per Cent
1925	Adams <sup>7</sup>	London Hospital	467	1919-1923	6.2
1925	Love <sup>8</sup>	St. Thomas Hospital	271	1919-1923	5.2
1927	Colp <sup>9</sup>	Mount Sinai Hospital, New York	975	1916-1926	3.1
1933	Walker <sup>10</sup>	Boston City Hospital	265	1927-1930	1.5
1933	Seelye <sup>11</sup>	Memorial Hospital, Worcester, Mass.	257	1929-1932	1.4
1934	Bower J. A. M. A. 102 813 (March 17) 1934	Philadelphia hospitals	3,317	1928-1932	2.50
1934	Garlock Am. J. Surg. 23 248, 1934	New York Hospital II Division	350	1928-July 1932	0.57

nish thought for means of prevention. Severe distention and ileus (mechanical in 2) developed in 7 cases, necessitating enterostomy or jejunostomy. This operation was usually done as a last desperate and final effort. It seems that jejunostomy might produce a more fortunate outcome if done earlier, as soon as other more conservative measures fail. This is one reason that enterostomy is condemned by many surgeons. One patient died of pylephlebitis, and in another the same complication developed together with a hepatic and subphrenic abscess. A secondary peritoneal abscess occurred in 2 cases. Urinary suppression was the cause of death in another case. Postoperative pneumonitis was a serious complication in 4 instances and undoubtedly the cause of death in 1. Drainage was established in all but 1 of the 10 cases at the original operation.

It seems that certain preventive measures might be instituted for lowering the mortality rate in this particular group. Great care should be given to the choice of an anesthetic, especially in the presence of an infection of the upper respiratory tract, emphysema, obesity and alcoholism. At the present time the use of spinal anesthesia, or avertin with nitrous oxide or local anesthesia seems highly desirable. Prevention of injury to the neighboring viscera and gentle removal of the appendix in order to avoid rupturing it are technical points which require no further comment. When there is actual difficulty in removing the appendix it might be wiser simply to insert a drain down to it, because if removal is attempted there may be considerable damage to the stump of the meso-appendix and the retroperitoneal tissues, thereby affording a means of extension of the infection and producing, possibly, pyelephlebitis, retroperitoneal cellulitis, phlebitis of the retroperitoneal veins and even septicemia. This certainly suggests itself as a possible cause in the 2 cases in which pyelephlebitis and hepatic abscess occurred. If enterostomy is to be employed it should be done early and not as an eleventh hour desperate measure. Lastly it is interesting to note that a number of patients with streptococcic appendicitis and local peritonitis give a history on admission of high fever, diarrhea and chill. These are the persons in whom a severe, overwhelming infection is likely to develop, with septicemia, pyelephlebitis, subsequent general peritonitis or paralytic ileus. They are the ones who need large amounts of fluids to combat the toxemia, and, equally important, they should receive repeated small blood transfusions (300 cc.) as a part of the supportive treatment.

If these few simple preventive measures are employed in this group of cases of appendicitis, it seems reasonable to suppose that the mortality rate will drop considerably more.

#### GROUP 3 ACUTE APPENDICITIS WITH PERITONEAL ABSCESS

*Definition*—In cases of acute appendicitis with peritoneal abscess the process has remained localized, as a rule, because of resistant forces which have prevented further spread of the infection. The abscess may be formed by any or all adjacent viscera, and its location depends, in large part, on the position of the appendix. The latter is usually found, in whole or in part, in the abscess cavity. It frequently reveals one or more perforations, and its surface may be covered with fibrin. There is often extensive gangrene, and sometimes the appendix may have partly or completely sloughed away. The contents of the abscess consist of thick, creamy, purulent exudate, containing fibrin and sometimes gas bubbles. The pus is often very odorous, and its color is yellowish, as a rule, although it may assume a greenish or even a brownish hue. Sometimes the abscess is very small and may contain 1 cc. of pus or less, more often one encounters several drachms or even several ounces of



pus The very large abscesses are seen (fortunately) with less frequency, but they sometimes acquire an enormous size, even larger than a baby's head In abscesses of recent formation the walls are apt to be made up of friable, edematous, easily bleeding tissue, and there is relatively little fibrin The adhesions between neighboring viscera, forming the wall of the abscess, can be separated with alarming ease In the larger and older abscesses the wall is often thicker, owing to considerable deposition of fibrin, frequently the fibrin gives a shaggy appearance to the inner surface of the wall of the abscess Here the adhesions of the surrounding structures are stronger, and if the operator (often

TABLE 7—*Annual Mortality Rate in Cases of Acute Appendicitis with Peritoneal Abscess at the Presbyterian Hospital*

Year	Number of Cases	Number of Deaths	Mortality, per Cent
1916	39	3	7.69
1917	40	1	2.50
1918	38	2	5.26
1919	44	7 (4)*	15.90
1920	43	9 (4)*	20.93
1921	37	3	8.10
1922	29	6 (2)*	20.68
1923	52	2	3.84
1924	42	6 (1)* (1)†	14.28
1925	27	2	7.40
1926	25	2 (2)*	8.0
1927	17	1	5.88
1928	12	0	0
1929	15	2 (2)*	13.33
1930	27	4 (2)* (1)†	14.81
1931	23	3 (2)*	13.04
1932	32	5 (2)*	15.62
1933	29	2 (1)*	6.89
Total	571 (492)* (490)†	60 (38)* (36)†	10.5 (7.72)* (7.34)†

\* See analysis of deaths, page 79

† See analysis of deaths, page 79

inadvisedly) digitally tears the wall of the abscess, there is less danger of bleeding and of spreading the infection One portion of the abscess is almost always formed by the parietal peritoneum, so that there may be considerable retroperitoneal cellulitis with thrombosis of the veins And this same condition often obtains for the thickened, edematous, friable, thrombosed meso-appendix Around the abscess there may be edema and congestion of the viscera, and one usually notes a small amount of free serous or slightly turbid peritoneal exudate If there has been extension of the infection through the wall of the abscess, there may be an associated diffuse (spreading) or even general fibrinopurulent peritonitis

*Mortality Rate*—Examination of table 7 and also of charts 5 and 6 shows a definite disturbing increase in the mortality rate in recent years Chart 6 illustrates this quite obviously, proceeding from a low level of

7.29 per cent in the period from 1925 to 1929 steadily upward to 12.69 per cent in the last five year period. While the average death rate in this group of cases is 10.5 per cent, there is reason to view this rise with alarm. On the other hand, the annual mortality rate discloses the lowest death rate in 1933 since 1928, and, if this can be maintained, the curve should begin to drop sharply.

*Comparative Study*—Table 9 discloses data from other hospitals and clinics for comparison with those from the Presbyterian Hospital. The



Chart 5—Graph showing the annual death rate from 1916 to 1933, inclusive, in 571 cases of acute appendicitis with peritoneal abscess. The total number of deaths was 60, the mortality rate, 10.5 per cent.

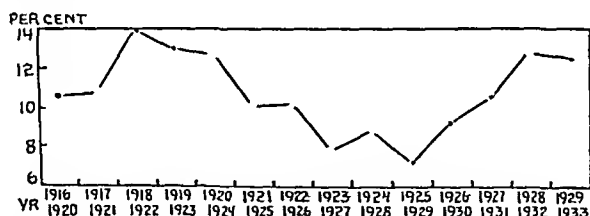


Chart 6—Graph for comparison with that in chart 5, showing the progressive five year death rate from 1916 to 1933, inclusive, in the same group of cases of acute appendicitis with peritoneal abscess.

mortality rate from the latter hospital is considerably higher than that given by Adams,<sup>7</sup> Love,<sup>8</sup> Colp,<sup>9</sup> Quam and Waldschmidt<sup>10</sup> and Bauer.<sup>11</sup>

7 Adams, J. E. Brit M J 1 723 (April 18) 1925

8 Love, R. J. Lancet 1 1229 (June 10) 1933

9 Colp, R. Ann Surg 85 257 (Feb.) 1927

10 Quam, E. P., and Waldschmidt, R. H. Acute Appendicitis. Report of 1,000 Consecutive Cases, Arch Surg 16 868 (April) 1928

11 Bauer, G. Acta chir Scandinav (supp 24) 70 1, 1933

Of particular interest is the report of Sworn and Fitzgibbon,<sup>12</sup> in which the death rate in a series of cases in which operation had been performed is compared with that in a series in which there was no operation. The nearest approach to this is the personal series of Guery,<sup>1</sup> with a mortality of 0.7 per cent. Seelye,<sup>13</sup> in a small group of cases covering a

TABLE 8—*Progressive Five Year Average Mortality Rates in Cases of Acute Appendicitis with Peritoneal Abscess at the Presbyterian Hospital*

Years	Number of Cases	Number of Deaths	Mortality, per Cent
1916-1920	204	22	10.78
1917-1921	202	22	10.89
1918-1922	191	27	14.13
1919-1923	205	27	13.17
1920-1924	203	26	12.80
1921-1925	187	19	10.16
1922-1926	175	18	10.28
1923-1927	163	13	7.97
1924-1928	123	11	8.94
1925-1929	96	7	7.29
1926-1930	96	9	9.37
1927-1931	94	10	10.63
1928-1932	109	14	12.84
1929-1933	126	16	12.69

TABLE 9—*Mortality Rate in Series of Cases of Acute Appendicitis with Abscess Reported in the Literature*

Year of Publication	Author	Place	Number of Cases	Period Studied	Mortality, per Cent
1925	Adams <sup>7</sup>	London Hospital	347	1919-1923	4.6
1925	Love <sup>8</sup>	St. Thomas' Hospital	95	1919-1923	4.2
1927	Colp <sup>9</sup>	Mount Sinai Hospital, New York	665	1916-1926	5.4
1928	Quain and Waldschmidt <sup>10</sup>	Bismarck, N. D.	289	1919-1927	2.42
1931	Tascho and Spano, Ann Surg 93:899, 1931	University Hospital, Minneapolis	112	1920-1929	9.7
1932	Sworn and Fitzgibbon <sup>12</sup>	St. Thomas' Hospital	189	1920-1929	7.9
		No operation	285	1920-1929	0.68
1933	Walker <sup>15</sup>	Boston City Hospital	328	1927-1930	9.7
1933	Bauer <sup>11</sup>	General Hospital, Malmo, Sweden	676	1903-1930	6.9
1934	Keyes, Ann Surg 99:47, 1934	Barnes and St. Louis Children's hospitals	315	1915-1932	7.3
1934	Garlock, Am J Surg 23:248, 1934	New York Hospital, II Division	51	1928-July 1932	11.76

period of only three years reported no deaths. The remaining observers, listed in table 9, reported a mortality comparable to that from the Presbyterian Hospital.

*Analysis of Deaths*—Of a total of 571 patients, 60 died. However, there were 77 patients who had acute diffuse peritonitis at operation, in addition to abscess,

12 Sworn, B. R., and Fitzgibbon, G. M. Brit J Surg 19:410 (Jan) 1932.

13 Seelye, W. C. New England J Med 208:123 (Jan 19) 1933.

and of these 20 died. Similarly, there were 2 patients with acute progressive fibrinopurulent peritonitis, together with abscess, and both died. On examining the records for these 22 fatal cases, there was no question but that death was due to the more serious diffuse, or fibrinopurulent, peritonitis, and not primarily to the abscess. These cases are listed under groups 4 and 5, where they properly belong, but they have also been placed in the present series in order to study appendical abscess as a whole and to avoid the criticism of deliberately trying to reduce the mortality rate for appendical abscess. For if these 79 records and the 22 deaths associated with them are excluded—and many might consider this as fair and justifiable—the mortality rate would be 7.72 per cent instead of 10.5 per cent (table 7\*). In addition to these 79 cases, there are 2 more which are certainly questionable when the cause of death is listed as appendical abscess. The first case was that of a woman aged 68, who was admitted to the hospital with a palpable appendical abscess. She had had a stroke three years before. The abscess was drained under infiltration with procaine hydrochloride, and the postoperative course was smooth until the occurrence of a cerebral accident on the tenth day. The patient became disoriented, confused and incontinent. Facial paralysis on the right side appeared on the sixteenth day, and she died of terminal bronchopneumonia three days later. Death can hardly be directly attributed to the peritoneal abscess.

The second case was that of a man aged 34, who was extremely ill and in a poor condition. An operation for an appendical abscess was performed at another hospital three months before. The patient was well for about a month and then began to have increasing fever and chills, together with intermittently draining sinuses. He was almost moribund when he entered the Presbyterian Hospital, and in spite of supportive treatment he died two days later. Autopsy revealed a subcecal abscess, thrombophlebitis of the pelvic veins, pyelophlebitis, abscess of the liver and bronchopneumonia. As this patient was operated on elsewhere and came to the hospital too ill for any further surgical intervention, it does not seem fair to include his case in computing the mortality rate of this group. If these 2 cases are excluded, as well as the 79 mentioned previously with 22 deaths, then the total number in this series would be 490 with 36 deaths, carrying a mortality of 7.34 per cent (table 7†). Nevertheless, these 24 fatal cases have been included in computing the following facts in the present death analysis.

Thirty-six of the 60 patients who died were males. Forty years was the average age, and only 18 were 30 years old or less. The youngest patient was 5½ years of age. The great majority of cases occurred in the fourth, fifth and sixth decades. The average duration of the present illness was six days. There was a recent infection of the respiratory tract in 9 cases, and active pulmonary tuberculosis in 2. Diabetes was present in 2 other cases, and marked obesity was observed in 10. A mass was felt in 25, and in 4 others it was detected on rectal examination only. During the first few years ether (by the open or closed method) was used, later, nitrous oxide, with or without ether, was used, and then ethylene, sometimes with ether. In more recent years, avertin or spinal anesthesia has been employed. Local infiltration with procaine hydrochloride has been employed only occasionally. The four most frequent sites of the peritoneal abscess were laterocecal, subcecal and retrocecal, mesocecal and pelvic. The abscess was described as "large" in 16 and "small" or "moderate-sized" in the remaining 44 patients. The appendix was removed in 45 of the 60 patients, removal was sometimes extremely difficult, thereby injuring natural barriers against the spread of the infection, often producing bleeding and lengthening the operating time considerably. The complications were chiefly intraperitoneal, pulmonary and vascular. An over-

whelming infection, with spreading peritonitis and severe toxemia, was described in 17. Distention was marked in 26 patients, and of these 14 had a paralytic ileus. Mechanical ileus developed in 5, and there was gastric dilatation in 6 others. Enterostomy was performed four times during the original operation and eleven times as a subsequent procedure. Secondary peritoneal abscess, usually late, occurred in 7 cases, and abscess of the liver was noted at autopsy in another 3. Of the 5 patients with pylephlebitis, 4 exhibited jaundice. Severe hemorrhage and disruption of the wound each occurred in 3 cases. Sixteen patients contracted postoperative pneumonitis, while 3 died of pulmonary tuberculosis. Four died of sudden fatal embolism. Severe profound shock was noted in 5. Pericarditis, suppurative parotitis and apoplexy were each present once. Two patients died of acidosis with diabetic coma, and 4 others of uremia. The great majority of these patients died within the first week or ten days.

A few cases deserve special mention. One patient underwent ileocelectomy because the inflammation, induration and thickening of the cecum and terminal portion of the ileum were interpreted as tuberculosis. This could not be substantiated by the surgical pathologist. Another patient suddenly went into a terminal toxic psychosis and died about a week later. A very interesting case was that of a patient admitted to the hospital with a diagnosis of pneumonia. The abdominal symptoms were completely masked by the pulmonary condition. The course was progressively downhill, with the development of marked distention. Roentgenograms failed to verify the clinical diagnosis of pneumonia. Finally, signs of subphrenic abscess appeared, and a transpleural thoracotomy was performed on the fifteenth day after admission. Autopsy on the following day revealed acute appendicitis with a pelvic abscess, abscesses of the liver and pylephlebitis. Another patient probably died from the premature injection of surgical solution of chlorinated soda (Dakin's solution) into the abscess cavity. A spreading peritonitis followed, and the patient died on the sixth day. A man, aged 63, came to the surgical service with a vague history of abdominal pain. A firm, rather tender mass was felt in the ileocecal region, and it was thought that it represented a carcinoma of the cecum. The patient was observed for eleven days. At operation a large retrocecal and laterocecal abscess was entered, obviously of appendical origin. The appendix was removed. Postoperative pneumonia soon appeared, jaundice developed on the fifth day, and the patient died the following morning. The record of a 17 year old boy is noteworthy. There was a history of illness of four days' duration which, combined with the physical examination, suggested a subsiding process. Because of an existing acute tonsillitis, it was considered safe to wait. On the tenth day sudden pain and cramps developed over the lower portion of the abdomen. Operation was immediately performed. A subcecal abscess was found. Appendectomy was very difficult. Marked distention and signs of spreading peritonitis set in the following day, to be followed by hiccup, vomiting and gastric dilatation. The patient died on the second day after operation. Another somewhat similar case was that of a woman, aged 79, with a history of abdominal pain of seven days' duration. She was very obese, and abdominal examination was extremely difficult to interpret. Operation followed three days later. The anesthetic was extremely poorly taken. The operator found a large retrocolic abscess, communicating with a mesocolic abscess. The appendix was removed. There was considerable retroperitoneal cellulitis in the vicinity of the abscesses. The patient died twelve hours later. Finally, one must not neglect to mention the case of a man who was operated on for acute appendicitis and drainage of a small pelvic abscess. Six days later signs of an acute mechanical ileus suddenly developed, and after all conservative measures failed to relieve him, he was taken to

the operating room to undergo jejunostomy. During the operation, while under anesthesia, the patient vomited and aspirated a considerable portion of the contents of the stomach. He died a few hours later from a fulminating aspiration pneumonia.

This analysis of the deaths and description of some of the cases constrains one to suggest certain preventive measures in trying to reduce the mortality rate. An older age group is being dealt with, which increases the hazard of operation and anesthesia. Would it not be wiser, therefore, to use local anesthesia oftener, especially in those cases in which a mass is palpable and in which it seems close to the anterior abdominal wall? Here, too, spinal anesthesia or avertin seems preferable to general anesthesia. In the operative procedure itself one should aim to create the least possible trauma and do the simplest and quickest sort of operation. Therefore, why not simply drain the abscess? Removal of the appendix under these circumstances is often difficult, it prolongs the operation and is fraught with dangers. It may provoke the inception of a retroperitoneal cellulitis, and often the trauma of appendectomy results in breaking through protective barriers. If the incision of choice is a right rectus incision, it is well to insert a few supporting stay sutures when sewing up the wound, because the distention, coughing, vomiting, straining and gastric lavage which often follow soon after operation may provoke disruption of the wound. By reason of the severe infection in these cases, it is probably better judgment not to approximate the subcutaneous tissues and the skin, these wounds should not be sewn too tightly. The surgeon must avoid the early irrigation of the abscess and wound with surgical solution of chlorinated soda, because there is great danger of producing a sudden spread of the infection into the general peritoneal cavity. One should wait at least five days after operation before instituting this procedure, and if its introduction causes severe abdominal pains it should be stopped at once. Because of the severe toxemia and infection, it is important that these patients receive large amounts of fluid by clysis, infusion, rectal tap and perhaps continuous intravenous drip. The fluid used should be chiefly a saline solution. One or more small transfusions are extremely helpful in combating an overwhelming infection and shock, one should not wait for complications to develop, one must learn to anticipate them and then direct one's efforts and therapy against their occurrence. If enterostomy or jejunostomy is planned, it should be done early and not after distention and paralytic ileus have existed for several days. One case of disruption illustrates the advisability of enlisting the support of a snug abdominal binder before performing a gastric lavage. In order to avoid aspiration pneumonia, it is extremely important to insist on a preoperative lavage in cases of ileus. Further, the 3 cases which were under observation before operation (described in the

analysis of deaths) emphasize certain definite risks and dangers in temporizing. Sometimes there is no other choice, the surgeon must learn to realize the gravity and seriousness of the situation and be prepared to intervene at once if the patient shows signs of spreading infection. Lastly, it is of the greatest importance to group the treatments with rest between times.

In this group also there was a relatively high incidence of pulmonary embolism and pyelephlebitis, this can be easily understood if the pathologic process of appendical abscess, as described in the preceding pages is accepted. Once more, therefore, let it be urged that the utmost gentleness be exercised in the operative procedure and an effort be made to avoid opening new avenues and routes to bacterial invasion. One must try to preserve the protective barriers already set up by the patient's resisting forces. One should help, not antagonize, nature's protective mechanism.

#### GROUP 4 ACUTE APPENDICITIS WITH ACUTE DIFFUSE (DIFFUSING, SPREADING) PERITONITIS

*Definition*—In this group of cases the process has spread from a state of local peritonitis, or of abscess formation, to one of extensive involvement of the abdominal cavity. The parietal and visceral peritoneum are usually edematous, markedly congested and somewhat friable throughout the operative field, perhaps all, or the greater part, of the celom is thus affected. The serosa of the abdominal viscera has lost its luster, and there may be moderate dilatation of the intestinal coils. Considerable purulent exudate is seen in all or most of the quadrants, it is usually thin and pale, but sometimes it is thick and creamy or reddish brown. The pus may be odorless, but frequently it is foul-smelling. As yet, there is little or no deposition of fibrin, so that few or no adhesions are seen, although there may be considerable fibrin with adhesions, in the vicinity of the appendix itself, especially if the diffuse peritonitis is preceded by the stage of abscess formation. The appendix may be partly or completely gangrenous and covered with shreds or plaques of fibrin. In the majority of cases, one or more perforations are seen in the appendix, and sometimes a fecolith may be discovered there. Not infrequently these fecoliths may be found in the abscess or in the peritoneal cavity. The meso-appendix is usually congested, thickened, edematous and very friable, and its blood vessels are often thrombosed. Retroperitoneal cellulitis may have developed around it. That portion of the cecum surrounding the base of the appendix may be indurated, edematous and congested, so that slight trauma may provoke tearing and bleeding of its serosa. The omentum also exhibits an extensive inflammatory reaction and it may have formed adhesions in the region of the appendix in its effort to localize

the infection. In short, the process has become a rapidly spreading or diffuse one, and pus is seen not only in the area about the appendix and pelvic cavity but also in the other quadrants, in the lumbar gutters and, occasionally, even in the subhepatic and subphrenic spaces.

Such an intra-abdominal pathologic process usually produces a fairly constant clinical picture. The patient looks acutely ill and often toxic, and the skin is hot and dry. The temperature is distinctly elevated and is between 101 and 103 F. The face is often flushed, and there may be slight dyspnea. Abdominal examination discloses a marked decrease, or an absence, of respiratory excursions. There are generalized involuntary muscle spasm, tenderness and rebound tenderness, and these

TABLE 10—*Annual Mortality Rates in Cases of Acute Appendicitis with Acute Diffuse Peritonitis at the Presbyterian Hospital*

Year	Number of Cases	Number of Deaths	Mortality, per Cent
1916	13	5	38.46
1917	17	3	17.64
1918	13	0	0
1919	20	6	30.0
1920	31	6	19.35
1921	19	1	5.26
1922	28	8	28.57
1923	20	2	10.0
1924	20	3	15.0
1925	16	0	0
1926	20	4	20.0
1927	14	2	14.28
1928	12	2	16.66
1929	14	3	21.42
1930	22	5	22.73
1931	15	2	13.33
1932	22	3	13.63
1933	12	1	8.33
Total	329	56	Average 17.02

signs may exhibit their maximum intensity in the right lower quadrant, suprapubic region or umbilical or periumbilical area, or more rarely in the right upper quadrant or left lower quadrant. This very fact alone, that the area of maximum intensity is not always found in the right lower quadrant, makes the early diagnosis in some of these cases extremely difficult. The appendix is often of the midline or pelvic type, thus favoring an easier and more rapid spread of the infection, so that there may be a complete lack of any localizing signs. It often requires great skill on the part of an experienced surgeon, let alone the general practitioner, to diagnose this condition early in its course.

*Mortality Rate*—The mortality rate is distinctly higher than that of the previous group (abscess), and a study of table 10 and charts 7 and 8 illustrates this clearly. Although the annual death rate percentages and the curve in chart 7 show a recent diminution in the



mortality, the progressive five year averages (table 11 and chart 8) are disturbing in that there is only a slight decline in the last three five year periods, and they do not compare favorably with some of the earlier ones. In fact, it is evident on studying the progressive five year average in table 11 and chart 8 that the mortality from acute appendicitis with

TABLE 11—*Progressive Five Year Average Mortality Rates in Cases of Acute Appendicitis with Acute Diffuse Peritonitis at the Presbyterian Hospital*

Years	Number of Cases	Number of Deaths	Mortality, per Cent
1916-1920	94	20	21.28
1917-1921	100	16	16.0
1918-1922	111	21	18.91
1919-1923	118	23	19.49
1920-1924	118	20	16.94
1921-1925	103	14	13.59
1922-1926	104	17	16.34
1923-1927	90	11	12.22
1924-1928	82	11	13.41
1925-1929	76	11	14.47
1926-1930	83	16	19.27
1927-1931	78	14	17.94
1928-1932	86	15	17.44
1929-1933	86	14	16.27

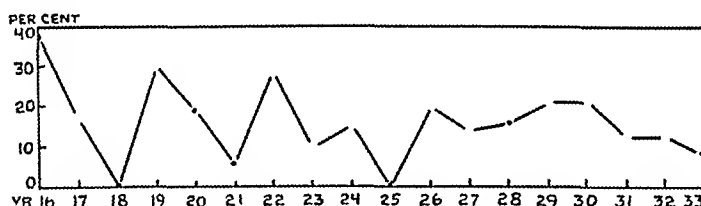


Chart 7—Graph showing the annual death rate from 1916 to 1933, inclusive, in 329 cases of acute appendicitis with acute diffuse peritonitis. The total number of deaths in this group was 56, the mortality rate, 17.02 per cent.

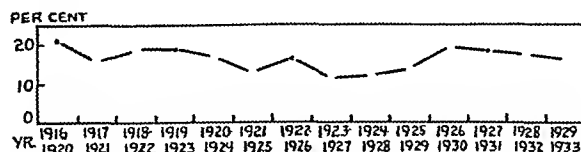


Chart 8—Graph for comparison with that in chart 7, showing the progressive five year average death rate in the same group of cases of acute appendicitis with acute diffuse peritonitis.

acute diffuse peritonitis has definitely increased when compared to the earlier five year periods between 1921 and 1929. The reader will note that the total average mortality rate of 17.02 per cent (table 10) is almost 1 per cent higher than that of the most recent five year period (16.27 per cent).

*Comparative Study*—The statistics for this group from the Presbyterian Hospital compare favorably with those of other investigators (table 12) Potter<sup>14</sup> reported a mortality of 35 per cent in 63 cases of acute appendicitis with acute diffuse peritonitis at the Bellevue Hospital, first surgical division, from 1920 to 1931. However, in the thirty-one months prior to the report of his most recent paper there was a mortality of only 15 per cent, which is about the same as that at the Presbyterian Hospital for that same period (12 per cent). Among those reporting a relatively large series of cases, only Bauer<sup>11</sup> and Walker<sup>15</sup> reported mortality rates which are lower than that at the Presbyterian Hospital. Many of the personal series, as well as those reported by a small limited group of surgeons, showed percentages as high or

TABLE 12—*Mortality Rates in Series of Cases of Acute Appendicitis with Acute Diffuse Peritonitis Reported in the Literature*

Year of Publication	Author	Place	Number of Cases	Period Studied	Mortality, per Cent
1925	Adams <sup>7</sup>	London Hospital	230	1919-1923	20.0
1925	Love <sup>8</sup>	St. Thomas' Hospital	187	1919-1923	29.4
1927	Colp <sup>9</sup>	Mount Sinai Hospital, New York	359	1916-1926	20.0
1928	Quain and Waldschmidt <sup>10</sup>	Bismarck, N. D.	160	1919-1927	10.0
1932	Sworn and Fitzgibbon <sup>12</sup>	St. Thomas' Hospital	231	1920-1929	20.0
1933	Bauer <sup>11</sup>	General Hospital, Malmö, Sweden	569	1909-1930	10.7
1933	Walker <sup>15</sup>	Boston City Hospital	204	1927-1930	11.8
1934	Bower, J. A. M. A. 102-813 (March 17) 1934	Philadelphia Hospitals	2,118	1928-1932	27.47
1934	Potter <sup>14a</sup>	Bellevue Hospital, I Division, New York	63	1920-1931	35.0
1934	Potter <sup>14b</sup>	Bellevue Hospital, I Division, New York	20	July 1931 to Feb. 1934	15.0

higher (Finney,<sup>2</sup> 22.08 per cent, Ashhurst,<sup>5</sup> 16.1 per cent, and Black,<sup>16</sup> 18 per cent). On the other hand, there are other personal series which are considerably lower (Dixon,<sup>3</sup> 10.4 per cent, Guery,<sup>1</sup> 8.2 per cent [16 per cent for the group in which operation was not performed], and Stoney,<sup>4</sup> 8.1 per cent).

*Analysis of Deaths*—The analysis of deaths and comments on possible means of mortality reduction in this very interesting and important group will be presented in detail in another paper. However, one may state that the outstanding measures of lowering the death rate in this particular group are adequate preoperative preparation, proper choice of anesthesia, the simplest operative procedure with minimum trauma,

14 Potter, P. C. (a) *S. Clin. North America* 14:379 (April) 1934, (b) *Ann. Surg.* 99:985 (June) 1934.

15 Walker, I. J. *New England J. Med.* 208:113 (Jan. 19) 1933.

16 Black, J. M. *Brit. J. M.* 2:1136 (Dec. 24) 1932.

speed (but not at the sacrifice of care and precision) and thoughtfully planned postoperative measures directed particularly against shock, distention and paralytic ileus and toxemia from an overwhelming infection. The recent papers by Jones, advocating appendicostomy, and by Easton and Watson, advising cecostomy or enterostomy, will be discussed in a later report. Here too, the treatments should be grouped together, so that the patient may obtain rest and sleep between times. The importance of team-work with the senior attending surgeons in the management of these cases cannot be too strongly emphasized.

GROUP 5 ACUTE APPENDICITIS WITH ACUTE GENERALIZED  
FIBRINOPURULENT PERITONITIS

*Definition*—Fortunately, only a few cases belong to this group. The condition represents the terminal stage of an uncontrolled, diffuse or spreading peritonitis. When one operates in such a case the pathologic process presents itself about as follows. There is edema of the deeper portions of the rectus abdominis muscle or the transversalis abdominis muscle, or both. The peritoneal tissues and transversalis fascia are likewise edematous and congested. The parietal peritoneum is thickened because of marked edema, injection and deposition of fibrin, these fibrinous areas often represent sites of adhesions between the parietal peritoneum and the abdominal viscera. The latter are likewise intensely inflamed, and the serosa no longer retains its smooth glistening surface but now appears red, roughened and angry. Fibrinous plaques and adhesions are seen everywhere between adjacent structures, and if these are separated, there will remain a bleeding, torn, friable, shaggy surface. Not only is there pus containing flakes of fibrin throughout the peritoneal cavity, but in addition the many adhesions tend to enclose small collections of similar exudate. The pus may be thick or thin and pale or creamy or blood-tinged, it sometimes has a strong, foul odor, and on other occasions it may be relatively odorless, in a few instances it has been described as producing a peculiar fishy smell. The appendix may have completely sloughed away, and fragments of it are sometimes floating in the purulent exudate. Evidences of previous earlier abscess formation may still be seen, and in certain instances one can detect the point of rupture with subsequent spreading and ultimate fibrinopurulent peritonitis. The intestinal coils are considerably dilated, as a rule, and the mesentery exhibits marked thickening from edema and infection. The mesenteric serosa is extremely friable and bleeds if torn. The mesenteric blood vessels, especially the veins, may be undergoing extensive thrombosis. There is almost always considerable retroperitoneal cellulitis in the vicinity of the appendix.

*Mortality Rate*—Of 25 patients with conditions of this type on whom operation was performed during the eighteen years of the present study

only 3 survived, producing a total average mortality rate of 88 per cent. The figures in tables 13 and 14 speak for themselves so that it is unnecessary to furnish mortality graphs.

TABLE 13—*Annual Mortality Rates in Cases of Acute Appendicitis with Acute Progressive Fibrinopurulent Peritonitis at the Presbyterian Hospital*

Year	Number of Cases	Number of Deaths	Mortality per Cent
1916	0	0	0
1917	1	1	100
1918	0	0	0
1919	4	4	100
1920	1	1	100
1921	2	1	50
1922	1	1	100
1923	2	1	50
1924	2	2	100
1925	0	0	0
1926	0	0	0
1927	3	3	100
1928	2	2	100
1929	1	1	100
1930	2	2	100
1931	1	1	100
1932	0	0	0
1933	3	2	66
Total	25	22	88

TABLE 14—*Progressive Five Year Average Mortality Rates in Cases of Acute Appendicitis with Acute Progressive Fibrinopurulent Peritonitis at the Presbyterian Hospital*

Year	Number of Cases	Number of Deaths	Mortality, per Cent
1916-1920	6	6	100.0
1917-1921	8	7	87.5
1918-1922	8	7	87.5
1919-1923	10	8	80.0
1920-1924	8	6	75.0
1921-1925	7	5	71.42
1922-1926	5	4	80.0
1923-1927	7	6	85.71
1924-1928	7	7	100.0
1925-1929	6	6	100.0
1926-1930	8	8	100.0
1927-1931	9	9	100.0
1928-1932	6	6	100.0
1929-1933	7	6	85.71

*Comparative Study*—Walker<sup>15</sup> reported a death rate of 33.3 per cent, Guerry<sup>1</sup> (personal series) gave the same figure, and Potter<sup>14b</sup> showed an average of 83.3 per cent (1920-1934, six cases with five deaths).

*Analysis of Deaths*—The 22 patients who died were almost equally distributed between the two sexes, 12 being males. The average age was 41, and there were only 6 patients under 30 years. The youngest was 7. Here again the highest

incidence fell into the fifth, sixth and seventh decades. The duration of the present illness varied from two days to eleven days, but most of the patients had a history of illness of two, three or four days' duration. The average duration was three and eight-tenths days. Three patients had an existing infection of the upper respiratory tract at the time of their admission, and another had active pulmonary tuberculosis. One patient had undergone an operation for acute osteomyelitis five days before and two days later complained of cramps in the lower portion of the abdomen and vomiting. The symptoms and signs were quite confusing, and it was only after general abdominal tenderness and rigidity developed that an acute abdominal condition requiring operation was recognized. Interestingly enough, the culture from the peritoneal exudate grew a different organism from that of the previous acute infection of the bone. In most of the cases a general anesthetic was used, especially the combination of nitrous oxide and ether. Local anesthesia was used only twice, and 3 other patients received spinal anesthesia. The duration of the operation varied from twenty to forty minutes in the majority of instances. Appendectomy was performed in 14 cases and enterostomy or jejunostomy in 5. Cecostomy was performed once. The postoperative complications were almost always severe. The overwhelming nature of the infection, with toxemia, distention and paralytic ileus, served to terminate life within a few hours or sometimes in one, two or three days. Fourteen patients died from general sepsis, 9 had marked distention and a paralytic ileus. Severe shock developed in 8, and acute gastric dilatation occurred in 4. Pulmonary edema was a terminal complication in 4 cases and pneumonitis in 7 others. There was complete urinary suppression in 3. Two patients died on the operating table. Secondary peritoneal abscess is recorded only once, because almost all these patients died shortly after the operation. Only 4 lived longer than three days. One patient died on the fifth day from urinary suppression, and at that time the peritoneal infection seemed to be controlled. The second patient, a boy of 14, lived eighteen days, peritonitis had subsided, but he failed to cooperate, and his activities provoked disruption of the wound. This was followed by severe secondary hemorrhage, resulting in shock and death in spite of several transfusions. In a third patient, the stormy postoperative period of distention and gastric dilatation had been surmounted. The patient seemed to be recovering, but at the beginning of the second week high fever developed, and the blood culture yielded a pure growth of the colon bacillus. Death intervened on the thirteenth day. The fourth patient had survived the severe reaction of the first week only to have an ischio-rectal abscess develop, which was incised and drained on the sixteenth day. Once again it appeared that he would recover, but on the twenty-fifth day there were signs of peritoneal abscess. It was drained through the old incision, but the patient failed to respond to supportive measures and died on the thirty-fourth day. He was 60 years old.

The treatment of these patients is extremely difficult because it requires careful judgment, based on experience. One must guard against too much therapy, yet it must be well directed against gastrointestinal, pulmonary and urinary complications. The proper choice of an anesthetic is extremely important here, perhaps spinal and local anesthesia could be employed a little oftener. Preoperative gastric lavage and clysis with saline solution before or during the operation are helpful in patients with marked distention and ileus. The operation should be done quickly, with the least possible trauma, and in most instances it is probably unwise to remove the appendix. One should be content to drain

the original focus or abscess and do no more. If the coils are markedly distended, jejunostomy or enterostomy can be quickly executed, and such a procedure should not be postponed until the patient is hopelessly beyond help. The postoperative care should consist of periods of adequate treatment, interspersed with several hours of sleep and rest, these sick patients cannot combat their infection without rest and plenty of it. Large amounts of fluids are most important, especially saline solution intravenously or subcutaneously, in order to supplant the loss of electrolytes incurred by the ileus and vomiting. The continuous intravenous drip is useful, but there is a real danger of giving too much, as this may precipitate acute pulmonary edema. The daily intake and output should be carefully recorded. The use of the nasal gavage tube will often prevent gastric dilatation resulting from regurgitation into the stomach of the contents of the duodenum and upper part of the intestine.<sup>16a</sup> Distention and paralytic ileus may be extremely difficult to handle, and the frequent use of abdominal poultices and the rectal tube, together with certain carminative enemas, may control it. Solution of pituitary or pitressin may be given with these treatments. Certainly there can be no danger of spreading the peritoneal infection any further. I have not been impressed with the effects of pitressin in cases of extensive peritoneal infection or of pronounced paralytic ileus. Transfusions and stimulants should be used before shock or collapse develops. The patients are probably more comfortable in a low or medium gatch position, and it is well to turn them at intervals as one means of preventing pneumonia and pressure sores. Hypertonic solution of dextrose (10 per cent) blood transfusions and hot colonic irrigations may be employed to combat renal suppression, although recently there is evidence at hand to indicate that saline solution is sometimes more efficacious than hypertonic dextrose solution. If the patient can be carried over this critical period, then one must prepare to meet other complications, such as secondary peritoneal abscesses, pyelephlebitis, subphrenic and hepatic abscess, hemorrhage and the lighting up of some latent disease process, such as pulmonary tuberculosis. The surgeon, therefore, should always endeavor to maintain a clear mental picture of the various

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16a Since this paper was written, some encouraging results have been obtained in cases with severe peritonitis and paralytic ileus by the combined use of the nasal gavage tube together with intravenous drip or infusion of a solution of alcohol in aqueous sodium chloride solution, as recommended by Dr. Sterling Mueller at the Bellevue Hospital, New York. It is prepared by adding 100 cc of 98 per cent alcohol to 900 cc of physiologic solution of sodium chloride. The nasal tube is connected to a water-suction apparatus so as to exert slight, continuous suction. This treatment will probably cut down the indications for jejunostomy for paralytic ileus. In a few cases it resulted in a striking and dramatic change in the patient within from twelve to twenty-four hours. The use of this alcoholic solution in saline usually results in a local thrombosis of the vein.

disease processes that are taking place and to give them their proper interpretation. In this manner his treatment will be rational and well directed and should yield the maximum benefit to his patient. There are, in addition, certain other preventive measures which will be discussed a little later.

*Cases of Survival*—The cases of the 3 patients who survived deserve brief mention. The first patient was a 12 year old boy with a history of illness of sixty hours' duration. A day after the onset of his illness, he took magnesium citrate. On admission, he looked acutely ill, and had a temperature of 103 F and a pulse rate of 130. The abdomen was rigid throughout, and there was diffuse tenderness,

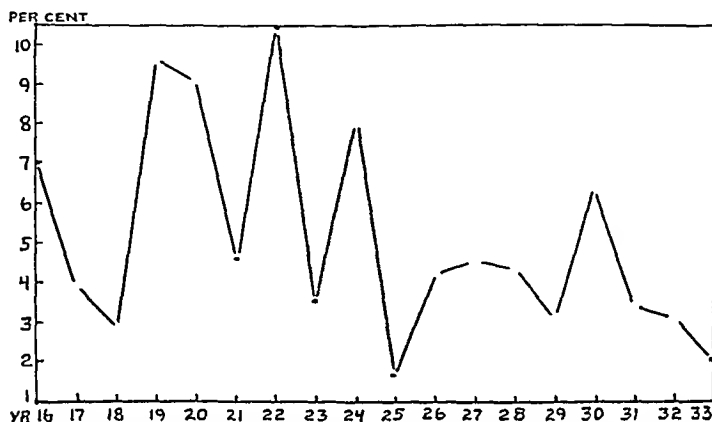


Chart 9—Graph showing the total annual death rate from 1916 to 1933, inclusive, in 2,653 cases of acute appendicitis with its associated lesions. The total number of deaths was 135, the total mortality rate, 5.08 per cent.

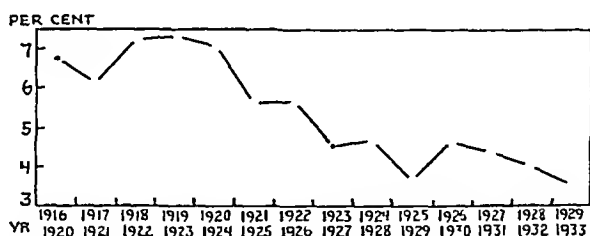


Chart 10—Graph for comparison with that in chart 9, showing the total progressive five year average death rate from 1916 to 1933, inclusive, in the same group of cases of acute appendicitis with its associated lesions.

perhaps a little more marked in the right lower quadrant and the suprapubic region. Rectal examination revealed tenderness high up on the right side. The white blood cells numbered 10,200, with 76 per cent polymorphonuclears. The pathologic process at operation was typical of acute progressive fibrinopurulent peritonitis. The appendix was procecal and entirely gangrenous. Culture of the pus showed *Bacillus acidilactici*, *Bacillus faecalis-alkaligenes*, *Streptococcus faecalis* and a gram-negative bacillus. A soft rubber tube was placed in the pelvis, and a cigaret drain was carried to the ileocecal region and another to the right lumbar gutter. There was a moderate reaction but no distention and only slight vomiting. Aside from the use of a poultice and a rectal tube, no rectal treatment was given until the seventh day,

when the patient received an enema. Daily hypodermoclyses and infusions were administered. Not a single complication developed. The patient was out of bed on the eighteenth day after operation and went home on the twenty-third day. A three year follow-up study showed him to be in excellent condition, symptom-free, with a firm scar.

The second case was similar to the first. The boy was 12 years old and gave a history of illness of five days' duration. He also took a strong cathartic a day after the onset of symptoms, following which his mother gave his abdomen a massage.<sup>1</sup> The pains were first in the lower portion of the abdomen, then they localized on the right side, and finally they became generalized. The boy looked acutely ill and had a temperature of 103.4 F and a pulse rate of 120. There were general abdominal rigidity and tenderness as well as rebound tenderness. The white blood cells numbered 20,000 with 96 per cent polymorphonuclears. At operation the appendix was as large as a man's thumb, and the distal third was wrapped in omentum. The pathologic process was one of acute progressive fibrinopurulent peritonitis. The nonhemolytic streptococcus and *Bacillus lactis-aerogenes* were cultured from the pus. One soft rubber tube and a cigaret drain were placed in the pelvis, and another soft rubber tube was carried to the right lumbar gutter. The patient reacted well. There was no vomiting and practically no distention. The first rectal treatment was given on the third day. Hypodermoclysis and infusion were given daily. Signs of a residual abscess in the left lower quadrant developed on the sixteenth day, but it seemed to resolve five days later. The patient was out of bed on the twenty-first day and went home on the thirtieth day. He was last seen at the follow-up clinic nineteen months after his operation, in good condition, with no complaints and with a firm scar.

The third case was that of a 22 year old man, with a history of illness of four days' duration. Following the onset of generalized abdominal cramps, he purged himself with salts and then proceeded to take three successive doses of castor oil (including a double dose!). There was no nausea or vomiting. He returned to work on the third day of his illness and went to a baseball game on the day of admission. He then consumed a large supper, and only because he vomited about an hour later did his mother bring him to the hospital. He looked very ill. The temperature was 102.4 F, and the pulse rate, 130. The abdomen was boardlike, yet the patient did not complain of tenderness anywhere, even on deep palpation. There was also absence of rebound tenderness. There was slight tenderness on rectal examination, high up anteriorly in the midline. The white blood cells numbered 12,700, with 74 per cent polymorphonuclears. At operation, one recognized typical progressive fibrinopurulent peritonitis. The omentum had covered the appendix, which was completely gangrenous and had perforated. About 1½ quarts of pus was aspirated. Only one organism grew from the culture, *Bacillus coli-communis*. One cigaret drain was introduced into the pelvis and another at the site of the appendix. There was a rather marked reaction but no vomiting. Pittressin, with the use of a poultice and a rectal tube, was given every four hours for three days, and this served to control the slight distention. Colonic lavages were administered a few times, and the patient received hypodermoclysis and infusion daily. The temperature was normal on the eighth day. All drains were removed on the eleventh day. On the thirty-third day he was out of bed, and he went home three days later. It is only five months since his operation, but so far the results have been entirely satisfactory.

The reader will observe that the patients who survived were males—2 boys and a young man. All took cathartics. In two instances the



total white cell count was relatively low, and the differential count was only slightly elevated. All patients had a surprisingly smooth post-operative course. The follow-up study, to date, has revealed most satisfactory results.

TABLE 15—*Total Annual Mortality Rates in All Cases of Acute Appendicitis and Associated Lesions at the Presbyterian Hospital*

Year	Number of Cases	Number of Deaths	Mortality, per Cent
1916	128	9	7.03
1917	128	5	3.90
1918	135	4	2.89
1919	133	13	9.77
1920	155	14	9.03
1921	150	7	4.66
1922	142	15	10.56
1923	167	6	3.59
1924	147	12	8.16
1925	122	2	1.63
1926	189	6	4.31
1927	131	6	4.58
1928	134	6	4.47
1929	159	5	3.14
1930	154	10	6.49
1931	149	5	3.35
1932	188	6	3.19
1933	192	4	2.08
Total	2,653	135	5.08

TABLE 16—*Progressive Five Year Average Mortality Rates in All Cases of Acute Appendicitis and Associated Lesions at the Presbyterian Hospital*

Years	Number of Cases	Number of Deaths	Mortality, per Cent
1916-1920	679	45	6.62
1917-1921	701	43	6.13
1918-1922	715	53	7.41
1919-1923	747	55	7.36
1920-1924	761	54	7.09
1921-1925	728	42	5.76
1922-1926	717	41	5.71
1923-1927	706	32	4.53
1924-1928	673	32	4.75
1925-1929	686	25	3.64
1926-1930	717	33	4.60
1927-1931	727	32	4.40
1928-1932	784	32	4.08
1929-1933	842	30	3.56

#### TOTAL MORTALITY RATE FOR GROUPS 1 TO 5

Table 15 and charts 9 and 10 are probably the most interesting of those shown, because they represent the total mortality rate in cases of acute appendicitis and its associated lesions. Whereas there is a certain factor of error in the data in the previous tables (as mentioned in the beginning of this report), the figures presented in tables 15 and 16

can be considered accurate. The total death rate has diminished in the past three years, and for 1933 (2.08 per cent) it is close to the record low level of 1925 (1.63 per cent). The progressive five year average of the total annual death rate shows a slight but definite decrease in the past seven periods as compared to the seven earlier ones (chart 10). The most recent one (1929 through 1933) discloses a record low level

TABLE 17—*Total Mortality Rates in Series of Cases of Acute Appendicitis and Associated Lesions Reported in the Literature*

Year of Publication	Author	Place	Number of Cases	Period Studied	Mortality, per Cent
1923	Lower and Jones J A M A 81: 629 (Aug 25) 1923	Cleveland	2,067	Not stated	3.1
1924	Deaver and Magoun Ann Surg 79: 834, 1924	Lankenau Hospital Philadelphia	5,488	1900-1920	5.0
1925	Adams <sup>7</sup>	London Hospital	1,677	1919-1923	5.8
1925	Love <sup>8</sup>	St. Thomas' Hospital	901	1919-1923	8.4
1927	Colp <sup>9</sup>	Mount Sinai Hospital New York	2,841	1916-1926	5.2
1928	Weeden Ann Surg 88: 76, 1928	New York Hospital	1,588	1914-1927	4.9
1931	Miller J Coll Surg Australasia 3: 40, 1931	Touro Infirmary and Charity Hospital, New Orleans	2,415	1924-1929	9.9
1931	McDonald Minnesota Med 14: 212, 1931	St. Mary's and St. Luke's hospitals, Duluth, Minn.	1,574	1925-1930	4.5
1932	Boland J A M A 99: 443 (Aug 6) 1932	Atlanta hospitals	4,270	1927-1932	4.4
1932	Raynor Proc Roy Soc Med 26: 181, 1932	Manchester Royal Infirmary	1,877	1928-1931	5.0
1932	Coit and Morrison Brit J Surg 20: 197, 1932	Aberdeen Royal Infirmary	1,349	1911-1930	5.5
1933	Bauer <sup>11</sup>	General Hospital, Malmö, Sweden	5,208	1903-1930	3.3
1933	Walker <sup>15</sup>	Boston City Hospital	2,106	1927-1930	5.8
1934	Bower J A M A 102: 813 (March 17) 1934	Philadelphia hospitals	14,904	1928-1932	4.79
1934	Nuttall Brit J Surg 21: 411, 1934	Liverpool Royal Infirmary	551	Not stated	2.5
1934	Garlock Am J Surg 23: 248, 1934	New York Hospital, II Division	1,188	1921-July 1932	4.7
1934	Keyes Ann Surg 99: 47, 1934	Barnes and St. Louis Children's hospitals	1,099	1915-1932	5.0
1934	Quain Arch Surg 28: 782 (April) 1934	Bismarck N. D.	1,000	Sept 1927 to Oct 1932	3.8

of 3.56 per cent, which is 1.5 per cent lower than that of the complete total of 2,653 cases with a mortality of 5.08 per cent.

This compares favorably with total mortality statistics in other hospitals (table 17). Some of the personal series had lower rates, for example: Guerry,<sup>1</sup> 1.1 per cent; Stoney,<sup>4</sup> 2.5 per cent; Hawe,<sup>6</sup> 4 per cent; Dixon,<sup>8</sup> 1.52 per cent; F. Angel and E. Angel,<sup>17</sup> 2.2 per cent; and Greenwood,<sup>18</sup> 0 per cent, (Greenwood cited a series of 206 cases covering

17 Angel, F., and Angel, E. South Med & Surg 95: 87 (Feb.) 1933

18 Greenwood, H. H. Lancet 1: 973 (May 11) 1929

a two year period only) Other authors reporting on personal series, or those representing cases observed by a small limited group of surgeons, submit mortality rates close to those of the Presbyterian Hospital Finney,<sup>19</sup> 4.92 per cent a few others give a higher rate, as Eliason and Ferguson,<sup>19</sup> 5.3 per cent and Warren,<sup>20</sup> 6 per cent

Chart 11 shows the curves of the five year averages in groups 1 to 4 and also that of the total mortality curve from 1916 to 1933 inclusive, thus enabling the reader to appreciate the relationships of the different groups to each other

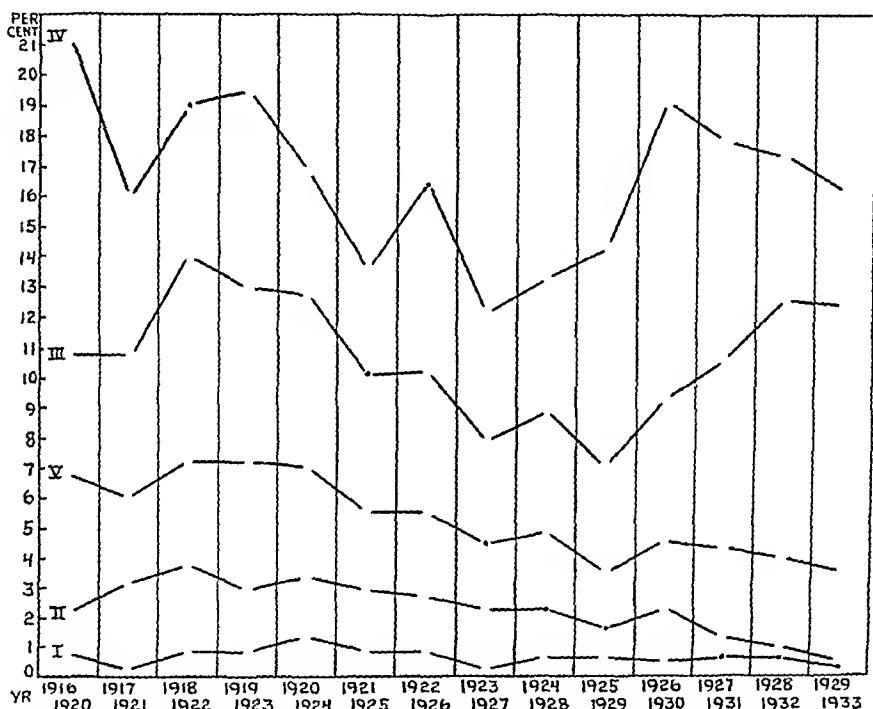


Chart 11—Graph showing the progressive five year average mortality curve from 1916 to 1933 for groups 1 to 4 and also the total progressive five year average mortality rate in all cases of acute appendicitis and its associated lesions. Curve I represents the cases of acute appendicitis, II, the cases of acute appendicitis with acute local peritonitis, III, the cases of acute appendicitis with peritoneal abscess, IV, the cases of acute appendicitis with acute diffuse peritonitis, and V, the total progressive five year average mortality rate of all cases of acute appendicitis and its associated lesions

#### COMMENT

The general mortality rate for acute appendicitis and its associated lesions at the Presbyterian Hospital has definitely declined. In separating

<sup>19</sup> Eliason, E. L., and Ferguson, L. K. *Ann Surg* 88:65 (July) 1928

<sup>20</sup> Warren, R. *Lancet* 2:16 (July 6) 1929

The original work on stainless steels was done by Brearley, Haynes, Cox, Hatch and Furness, and the generic term stainless steel was applied to the steel covered by their patents. These early steels contained chromium alone. The chrome-nickel steels were of a later vintage. Popular usage has caused all corrosion-resisting steels to be known as rustless steel regardless of their chromium or nickel content.

From the almost innumerable varieties of rustless steels three were chosen which are fairly representative of the group. The first is high in chromium content with nickel entirely absent. It will henceforth be designated as nickel-free rustless steel. The approximate composition is as follows:

Substance	Percentage
Carbon	0.10, maximum
Manganese	0.30-0.60
Silicon	0.30-0.50
Phosphorus	0.03, maximum
Sulfur	0.30-0.45
Molybdenum	0.55 (approximate)
Chromium	14.00-15.50

The second alloy chosen is low in chromium content and high in nickel content, the proportion being about 1:3. It is termed high nickel rustless steel in this text. The approximate composition is as follows:

Substance	Percentage
Carbon	0.300-0.50
Manganese	0.600-0.90
Phosphorus	0.035
Sulfur	0.035
Silicon	1.250-1.50
Copper	1.000-1.50
Chromium	7.500-9.00
Nickel	21.500-23.50

The third alloy tested is high in chromium content and low in nickel content, the proportion being about 2:1. For this reason it is called low nickel rustless steel. The approximate composition is as follows:

Substance	Percentage
Carbon	0.700, maximum
Manganese	0.400-0.65
Phosphorus	0.035
Sulfur	0.035
Silicon	0.300-0.75
Nickel	8.000-9.50
Chromium	17.500-19.00

Low nickel rustless steel showed a reaction but one of greatly diminished intensity when compared with that of the first two alloys described. The zone of reaction was extremely narrow. Microscopically, the defect was lined by a thick fibrous tissue layer which showed marked hyperemia. There was a small amount of hemorrhage accompanied by slight lymphocytic infiltration. The bony trabeculae immediately adjacent to the defect showed rarefaction by osteoclasts.

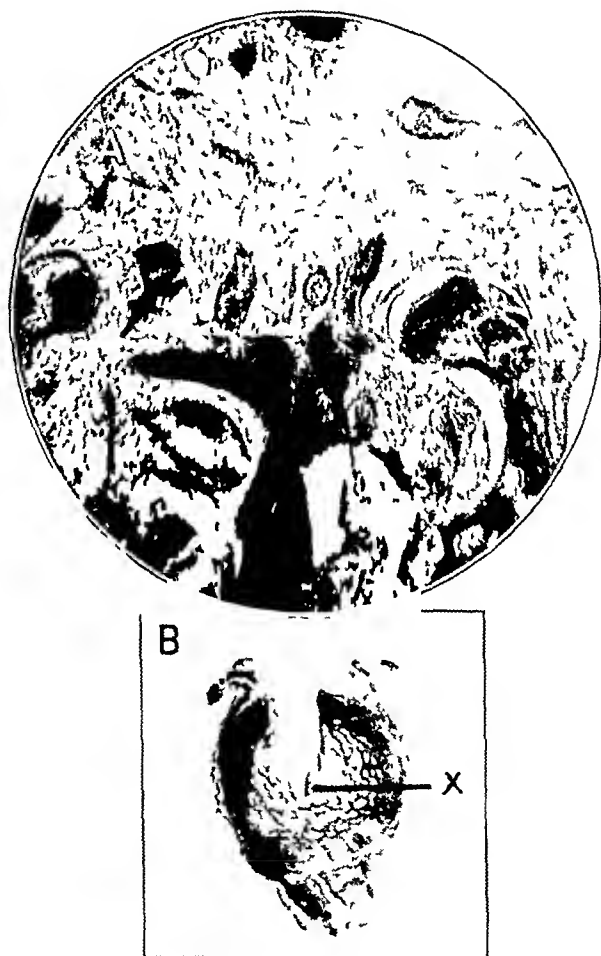


Fig 6—*A*, high power photomicrograph, showing reaction of bone to low nickel rustless steel after the tack remained thirty days in the tibia. *B*, low power photomicrograph, indicating almost complete absence of a fibrous capsule, *x* marking the site shown in *A*. This demonstrates a lesser amount of cellular reaction and generalized fibrous osteitis in medullary spaces, retention of trabecular structure and minimal destruction of bone.

The marrow throughout the entire section showed extensive fibrosis, some hyperemia with small hemorrhages and a scanty lymphocytic infiltration. The general picture resembled that of fibrous osteitis.

The physical properties of these three rustless steels vary. The alloy that is free from nickel is soft and easily machined. The two alloys containing nickel are very hard and become even harder during the process of cold-machining (austenitic property). Thus they require special tools for fabrication. For this reason any order addressed to a manufacturer for a prosthesis without specification of the exact formula of rustless steel desired will invariably be filled from the more easily machined nickel-free types. Investigation shows that practically all the appliances at present are made of rustless steels having approximately the first formula. In the light of the results that follow, this point should be remembered.

Through the courtesy of the chemical laboratories of the Vanadium Steel Corporation of America and the Crucible Steel Corporation of America, samples were furnished having the formulas just given. From these, tacks were accurately machined. The shape is adequately shown in figure 1. The measurements were diameter of the head, 0.125 cm., diameter of the shaft, 0.1 cm., length of the shaft, 0.725 cm.

#### EXPERIMENTAL PROCEDURE

The experimental procedure in general consisted in weighing the tacks and then under aseptic precautions placing them in the bones of dogs. The reaction of the metal to the bone was studied by removing the tack, again weighing it and computing the loss of weight. The reaction of the bone to the metal was observed by fixing, sectioning and studying the defect in the bone created by the tack. Control holes were made for the purpose of studying the reaction of bone to a drill hole. Only large adult dogs were selected.

Dog 1—This animal was a female police dog of mixed breed, about 1½ years old, weighing about 22 Kg. The central portions and the inside surfaces of both tibias in the midportions and the lateral surfaces of both femurs were exposed through incision. The periosteum was excised and retracted. A drill having a slightly smaller diameter than the shaft of the tack was used to perforate the cortex. The tacks selected were then lightly driven into this opening until the top of the head was flush with the periphery of the bone. In this experiment the tacks had the following locations: nickel-free rustless steel tack, right tibia; vanadium steel tack, left tibia; high nickel rustless steel tack, right femur; low nickel rustless steel tack, left femur. The periosteum and skin were closed in separate layers.

Dog 2—This animal was a male dog of mixed breed, predominantly collie, about 2 years old, weighing about 24.5 Kg. In a manner exactly similar to that already described the tacks were placed in the following locations: low nickel rustless steel tack, right tibia; high nickel rustless steel tack, left tibia; nickel-free rustless steel tack, right femur; vanadium steel tack, left femur. In these two experiments the tacks were allowed to remain in situ for thirty days, and the dogs were then killed.

The reaction of this metal was observed in another section to show that there are slight variations in results even when the same metal is used. In this instance the defect was lined by a wide layer of fibrous tissue. The surrounding bone marrow showed extensive fibrosis accompanied by only slight hyperemia, and scattered hemorrhages. The remaining bone marrow was entirely free from changes. Only the bone trabeculae immediately adjacent to the peg hole showed slight osteoclasia.

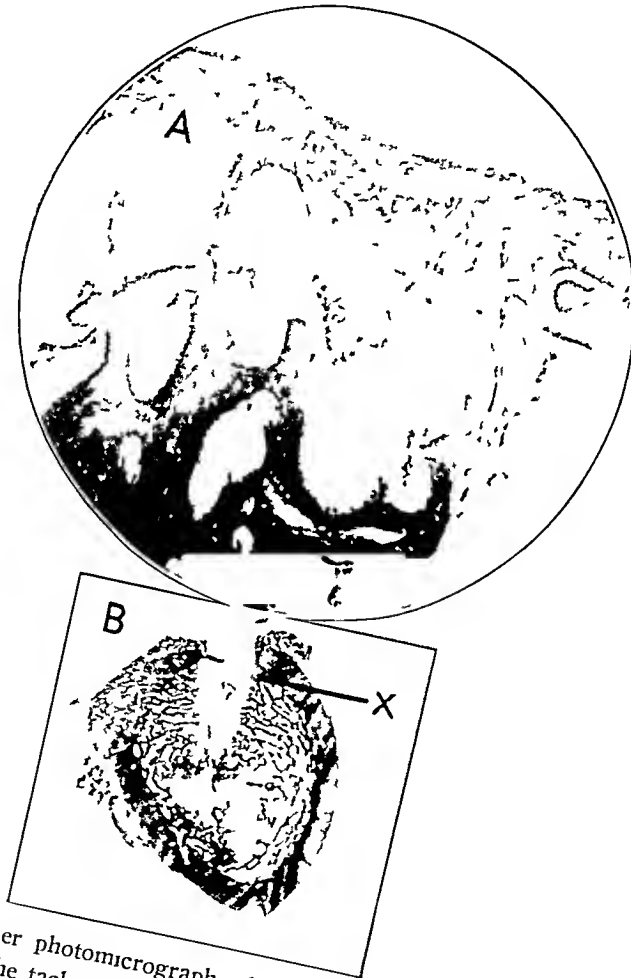


Fig 7—*A*, high power photomicrograph, showing reaction of bone to nickel-free rustless steel after the tack remained thirty days in the femur. *B*, low power photomicrograph, illustrating minor variations in the reaction, even when the same metal is used (see figure 6). Here there is the formation of a thin fibrous capsule, with almost complete absence of medullary reaction or fibrosing osteitis.

#### COMMENT

At the beginning of this article two postulates were proposed which we felt to be essential to any studies concerned with the interaction of bone and metal. The first of these original premises is confirmed, viz.,

Dog 3—This animal was a large male "bull-police" dog, 3 years old, weighing 27 Kg

The internal surfaces of both tibiae were exposed for a distance of about  $2\frac{1}{2}$  inches (6.4 cm), and four drill holes were made  $\frac{1}{2}$  inch (1.3 cm) apart, in the longitudinal plane. The tacks on both sides from above downward were, in order of appearance: vanadium steel tack, nickel-free rustless steel tack, low nickel rustless steel tack and high nickel rustless steel tack. These were allowed to remain in place for forty days.

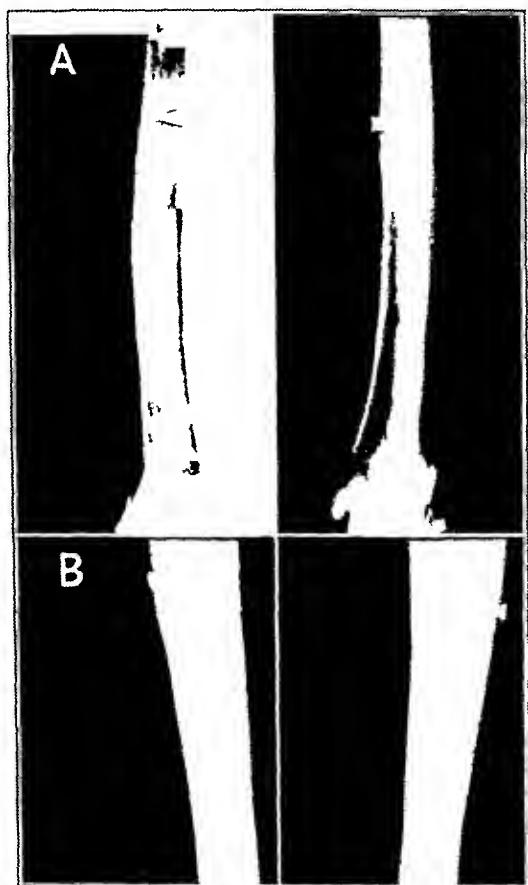


Fig 1—Roentgenograms of (A) both femurs and (B) both tibiae of dog 1, taken thirty days after the insertion of the tacks. There is a marked periosteal reaction in the left tibia about a vanadium steel tack, with no demonstrable roentgenographic reaction about the other tacks.

Dogs 4 and 5—The studies on these animals were started at the same time as the experiment on dog 3 and were performed in an exactly similar manner. Four tacks were placed in the central portions of both tibiae of these dogs. At the time that dog 3 was killed certain phenomena of loss of weight of the metal were becoming apparent. It was deemed inadvisable to kill the dogs at this time, without the insertion of more samples.



that the exact chemical composition of any metal used for osteosynthesis should be known. This is true for two reasons, namely, that comparable experimental results by different observers demand this knowledge and that alloys of the same generic name may vary so widely in chemical composition as to give entirely dissimilar physiologic effects. The stellite or "rustless steel" used by Zierold was erroneously assumed to be a chrome or chrome-nickel alloy. The exact formula for a number of stellites was obtained only after prolonged investigation by the Haynes Stellite Company and after the conclusion of this experiment. Misapprehension as to the "rustless steel" used by Zierold has been shared generally, as the one in common use is an alloy of an entirely different composition and one that corrodes easily in bone. The original stellite used in his experiments is probably as nonirritant as the chrome-nickel alloys, as it resists corrosion in Ringer's solution quite as effectively.

The second postulate is that the reaction of metal to bone should be studied as well as the reaction of bone to metal. A metal should not be used for osteosynthesis which corrodes rapidly in body fluids. The simple test of first immersing it in Ringer's solution is one that should precede *in vivo* experiments or clinical use. It is significant and important clinically that the major portion of the loss of weight occurs early. It is during this period that fixation of bone becomes unstable. The joint effects of shrinkage of the prosthesis and of bone necrosis occur at the very period when firm support is most desired.

The portion of the experiment on the reaction of bone (third postulate) is incomplete. Undoubtedly, certain metals are relatively or completely nonirritant to the individual osteoblasts and fibroblasts. The opinion persists that the mass of a foreign body may be sufficient to interfere with the blood supply, causing reaction in varying degree. The experiment will be continued in an attempt to test the reaction of bone to objects of graded sizes.

It follows that all the mentioned factors are equally concerned in causing the complex set of phenomena which have been designated bone-metal interaction. The results of this experiment permit certain suppositions as to the train of events. Loss of weight of metal proceeds at a more rapid rate in bone than in Ringer's solution. This indicates that there is an additional factor which adds to the effect produced by the electrolytes contained in the tissue fluids. The accelerated rate of corrosion *in vivo* is probably due to the defensive reactions set up in the richly cellular bone marrow. With increasing corrosion and precipitation of irritant particles there is greater reaction of bone. The circle is finally broken with the formation of a fibrous tissue capsule and the complete encystment of the foreign body. The end-result is a corroded

## ARCHIVES OF SURGERY

Dog 4—This animal was a female collie of mixed breed, aged 3 years, weighing 135 Kg. The tacks from above downward in the central portions of both tibias were, in order of appearance: vanadium steel tack, nickel-free rustless steel tack, low nickel rustless steel tack and high nickel rustless steel tack. At the end of the forty day period, which had marked the killing of the third dog, additional tacks were inserted in the following locations: two tacks of low nickel rustless steel in the lower external surface of the right and the left humerus, and two tacks of low nickel rustless steel just below the trochanters of both femurs, and two tacks of low nickel rustless steel were placed. At the lower internal surface of each tibia, the left femur. In the external surface of the lower ends of both femurs two vanadium steel tacks were inserted. At the end of in situ, two tacks of high nickel rustless steel were inserted. At the end of in additional forty-five days the dogs were killed, and the tacks and the specimens of bone were obtained. Thus the eight tacks in the central portions of the tibias remained seventy-five days, all the others remained thirty days.

Dog 5—This animal was a female halfbreed police dog, aged about 2 years, weighing about 23 Kg. The procedure of this experiment was similar to that of the foregoing in that at the first stage the central internal surfaces of both tibias were exposed and four tacks at  $\frac{1}{2}$  inch (1.3 cm) distance from each other were inserted in the usual manner. On both sides the order from above downward was: vanadium steel tack, nickel-free rustless steel tack, low nickel rustless steel and high nickel rustless steel. At the end of thirty days additional tacks were placed in the following locations: vanadium steel tack, lower end of the right humerus, nickel-free rustless steel tack, lower end of the left humerus, high nickel rustless steel tack, just below the trochanter of the right femur, low nickel rustless steel tack, just below the trochanter of the left femur, low nickel rustless steel external surface of the lower end of the right femur, vanadium steel tack, external surface of the lower end of the left femur, high nickel rustless steel tack, internal surface of the lower end of the right tibia, about 2 inches (3 cm) below the tacks previously inserted, and nickel-free rustless steel tack in the same location on the left side. The time elements in the experiments on dogs 4 and 5 were exactly similar.

## OBSERVATIONS

As certain of the metals caused considerable periosteal reaction, it was often quite a problem to remove the tacks without causing injury to them or to the specimens of bone. Certain minor variations in loss of weight are accounted for by this factor. For this reason a number of the tacks were selected with which there was no possibility of gross technical error in the computation of post-operative weight. Another reason for exclusion was the complete or partial extrusion from the bone.

Inspection of the tables show that the major portion of the loss of weight occurred within the first thirty days. It was also noted that the loss of weight was not affected by the close proximity of one tack to another or by the location of the tack in various bones. Two sets of tacks, one of vanadium steel and the other of nickel-free rustless steel, when isolated from other tacks, were extracted from the bone without

and shrunken prosthesis lying loosely in an osseous defect made larger by necrosis of bone. Thus, the hypothesis is proposed that the intensity of reaction of bone is directly proportional to the chemical changes that occur in the metal with which it is in contact.

## CONCLUSIONS

When a metal subject to corrosion is inserted into bone, a complex set of phenomena arise which has been termed bone-metal interaction. This experiment shows that the reaction of bone is linked with metallic corrosion.

Four metals were chosen for investigation, among them a specific alloy of vanadium steel prescribed for the standard Lane plate. Rapid corrosion and extensive necrosis of bone combine to contraindicate its use for osteosynthesis.

Nickel-free rustless steel, a metal widely used at present in bone prostheses, is placed in the same group. The same effects follow its use in only a slightly less degree.

The chrome-nickel rustless steels are the metals of choice. Corrosion of these alloys is minimal. Although they are not completely nonirritant in bone, their use is recommended.

TABLE 1—*Loss of Weight of Inadnum Steel*

Pin	Dog	Bone	Weight of Tack, Gm		Percent age of Loss	Days in Bone	Comment
			Before Insertion	After Removal			
1	4	Tibia	0.242	0.221	8.60	75	Profuse hemorrhage from marrow
2*	4	Tibia	0.251	0.231	7.90	75	Extruded from bone
3*	3	Tibia	0.256	0.235	8.20	40	Heavy periosteal overgrowth
4*	3	Tibia	0.262	0.235	10.50	40	Tack injured in removal, heavy overgrowth of bone
5*	5	Tibia	0.262	0.241	10.20	75	Tack injured in removal dense osteoperiosteal overgrowth
6	5	Tibia	0.264	0.244	7.60	75	Dense osteoperiosteal overgrowth
7	4	Femur	0.275	0.255	7.20	30	Slight periosteal overgrowth
8	4	Femur	0.278	0.254	8.60	50	Slight periosteal overgrowth
33	5	Humerus	0.200	0.181	9.50	30	Covered with soft loose periosteum
34	5	Femur	0.200	0.185	10.00	30	Slight periosteal overgrowth
36	2	Femur	0.231	0.210	9.09	30	Slight periosteal overgrowth
39	1	Tibia	0.207	0.217	6.56	30	Slight periosteal overgrowth

\* Excluded from the final computation.

TABLE 2—*Loss of Weight of Nikel-Fire Rustless Steel*

Pin	Dog	Bone	Weight of Tack, Gm		Percent age of Loss	Days in Bone	Comment
			Before Insertion	After Removal			
9	4	Tibia	0.276	0.254	7.90	75	Slight periosteal reaction
10	4	Tibia	0.279	0.256	8.10	75	Periosteal overgrowth
11	3	Tibia	0.272	0.245	9.90	40	Osteoperiosteal overgrowth
12*	3	Tibia	0.269	0.245	8.90	40	Extruded from the bone
13	5	Tibia	0.275	0.254	7.60	75	Dense osteoperiosteal overgrowth
14	5	Tibia	0.280	0.274	1.90	75	Dense osteoperiosteal overgrowth
15*	4	Femur	0.287	0.265	7.00	30	Extruded from the bone
16	4	Femur	0.272	0.267	1.70	30	Slight periosteal reaction
40*	5	Tibia	0.221	0.220	0.67	30	Extruded from the bone
41	5	Humerus	0.241	0.230	4.70	70	Periosteal overgrowth
42	2	Femur	0.252	0.251	0.19	70	Slight periosteal reaction
45	1	Tibia	0.291	0.270	7.21	50	Slight periosteal reaction

\* Excluded from the final computation.

TABLE 3—*Loss of Weight of High Nickel Rustless Steel*

Pin	Dog	Bone	Weight of Tack, Gm		Percent age of Loss	Days in Bone	Comment
			Before Insertion	After Removal			
17*	4	Tibia	0.242	0.241	0.20	75	Extruded from the bone
18*	4	Tibia	0.245	0.235	2.80	75	Tack injured in removal, periosteal overgrowth
19	3	Tibia	0.240	0.245	1.60	40	Thin bony overgrowth
20	3	Tibia	0.251	0.246	2.15	40	Dense periosteal overgrowth
21	5	Tibia	0.256	0.255	0.39	75	Slight periosteal reaction
22	5	Tibia	0.257	0.254	1.0	75	Slight periosteal reaction
23	4	Humerus	0.259	0.251	1.70	30	Slight periosteal reaction
24	4	Humerus	0.260	0.260	0	30	Slight periosteal reaction
46*	5	Femur	0.220	0.216	1.80	30	Extruded from the bone
47*	5	Femur	0.225	0.228	0	70	Extruded from the bone
48*	2	Tibia	0.232	0.226	2.79	30	Tack injured in removal
52	1	Femur	0.238	0.234	1.85	30	Slight periosteal reaction

\* Excluded from the final computation.

# TRUE HOUR-GLASS BLADDER

## A CONSIDERATION OF ITS ETIOLOGY AND TREATMENT

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The term hour-glass bladder has been used to designate a number of different pathologic and clinical entities. In this communication we shall not consider those cases included in Blum's<sup>1</sup> classification under type III, namely, the acquired variety due and subsequent to severe trauma, ulceration, operation, cicatricial contraction, tuberculosis or other inflammatory processes. We shall likewise not consider those cases of diverticula of the bladder erroneously reported as hour-glass bladder. The patient whom we have studied and operated on presented what Kretschmer and Morris<sup>2</sup> have called a true hour-glass bladder, regarding which there are but few reports in the literature. Young<sup>3</sup> described the condition as "one in which the bladder is circularly constricted and divided into two portions with a narrow canal of communication as in an hour-glass." He stated that he had operated on a patient in whom the circle of contracture passed across the posterior wall of the bladder at least 1 inch (2.5 cm.) behind the trigon. It is this type, in which the ureters enter the lower chamber of the bladder, which we are to describe and relating to which there are authentic reports by Fothergill,<sup>4</sup> Passow,<sup>5</sup> Muller,<sup>6</sup> Caulk,<sup>7</sup> Kretschmer and Morris<sup>2</sup> and Young<sup>3</sup>. Certain other reports do not state into which chamber the ureters entered and must therefore be excluded from this category.

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1 Blum, V. *Chirurgische Pathologie und Therapie der Harnblasendivertikel*, ed 2, Leipzig, Georg Thieme, 1929, p. 58.

2 Kretschmer, H. L., and Morris, H. L. *J Urology* **10** 181 (Aug.) 1923.

3 Young, Hugh, and Davis, D. M. *Young's Practice of Urology*, Philadelphia, W. B. Saunders Company, 1926, vol 2, p. 371.

4 Fothergill. *Mem. Neurol. Soc. London*, vol 1, 1878, quoted by Caulk.<sup>7</sup>

5 Passow. *De hypertrophia parietum vesicae urinae*, Inaug. Dissert., Vratislaviae, 1848, quoted by Caulk.<sup>7</sup>

6 Muller, B. *Ein Fall von Missbildung am Beckenteil des weiblichen urogenital Apparates*, Inaug. Dissert., Marburg, 1895.

7 Caulk, John R. *Ann. Surg.* **71** 22 (Jan.) 1920.

difficulty, whereas the tacks of high nickel rustless steel and low nickel rustless steel were firmly held

In addition to the fact that all the vanadium steel tacks were loose in the bone, an outstanding observation was the blackish discoloration of the tack hole and of the surrounding soft parts

Loss of weight was high, as in the eight tacks listed in table 1 There was an average reduction of 8.38 per cent from the original mass

In the case of nickel-free rustless steel, nine tacks were used, with an average loss of weight of 7.03 per cent (table 2)

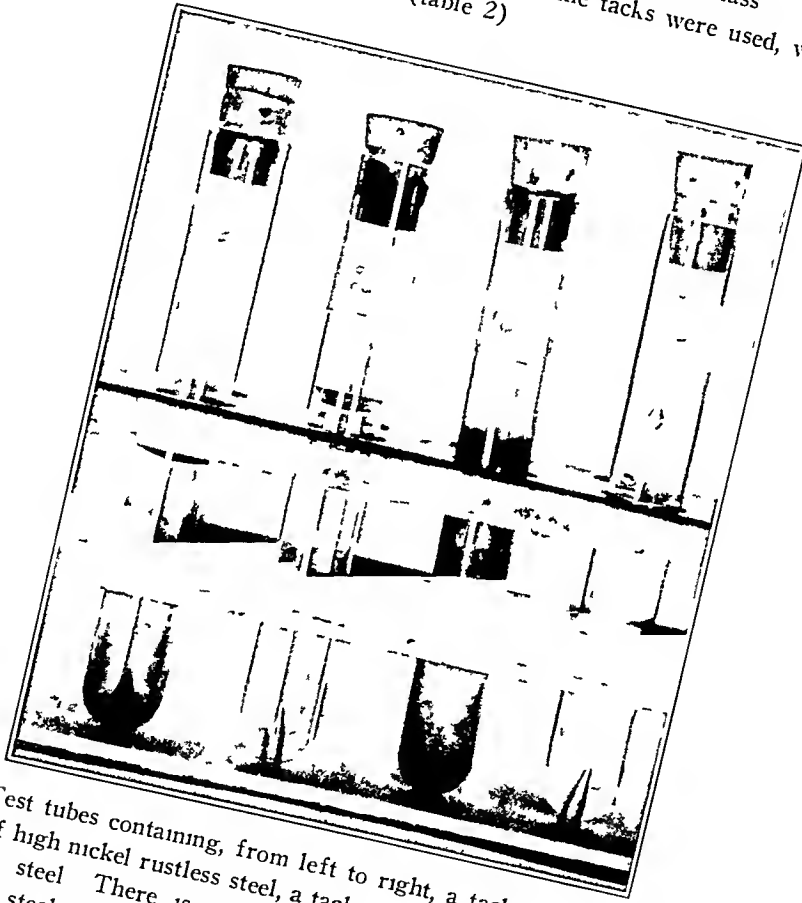


Fig 2—Test tubes containing, from left to right, a tack of nickel-free rustless steel, a tack of high nickel rustless steel, a tack of vanadium steel and a tack of low nickel rustless steel There is complete absence of corrosion of both chrome-nickel rustless steels The heavy precipitate in the first and third tubes illustrates the extensive corrosion of nickel-free rustless steel and vanadium steel by Ringer's solution

The difference in loss of weight when the nickel-free rustless steel and the chrome-nickel alloys are compared is enormous High nickel rustless steel had a loss of weight of 0.125 per cent in seven tacks, and low nickel rustless steel, a loss of weight of 0.8 per cent in nine tacks (tables 3 and 4)

The phenomenon of early and rapid loss of weight in two of the metals tested and of relatively little loss of weight in the others led to speculation as

Cases of true hour-glass bladder in which the ureters entered the upper chamber have been reported by Fuller,<sup>8</sup> Detweiler<sup>9</sup> and Cutter<sup>10</sup>

This apparently rare anomaly has more than an academic interest for the urologist because of the need of an accurate diagnosis in certain cases of dysfunction of the bladder, as well as the necessity of rational surgical treatment when a diagnosis is made. The relationship between true hour-glass bladder and certain examples of transverse folds of the bladder must necessarily be explored, and we are fortunate in having two instances of transverse folds under observation at present. Zuckerkindl,<sup>11</sup> writing of transverse folds, said "If they appear higher, that is, above the linea interureterica, and are raised to form sickle-like configurations and involve a greater portion of the periphery, they actually become a diaphragm resulting in hour-glass bladder."

#### ETIOLOGY

A careful survey of the few clinical reports available reveals almost total absence of reference to the etiology of this condition. In fact, discussion thereof in most communications is entirely omitted. Gruber<sup>12</sup> stated that certain types of hour-glass bladder occur as a result of excessive growth of tissue of mesodermal origin producing sickle-shaped horizontal folds. Delbet<sup>13</sup> said that the transversely bisected bladder indicates, in his opinion, the correctness of the modern point of view regarding the development of the bladder and that the contraction which occurs above the entrance of the ureters into the bladder is due to a local hypertrophy of the circular musculature of the bladder. Orth<sup>14</sup> designated the pathologic condition as a partial stricture of the middle portion of the bladder, and Pagenstecher<sup>15</sup> said that the condition which is most correctly termed "congenital hour-glass bladder occurs in cases in which anatomically and functionally different components meet or border on each other and results from the unequal growth of the normally separate bladder anlagen, which are noted in embryos 17 mm

8 Fuller, E. J. *Cutan & Genito-Urin Dis* **18** 531 (Dec.) 1900

9 Detweiler, E. L. *An Hour-Glass Bladder*, *Virginia M. Monthly* **15** 644, 1888-1889

10 Cutter. *Lancet* **1** 185, 1854

11 Zuckerkindl, O., and von Frisch, A. *Handbuch der Urologie*, Vienna, A. Holder, 1903, vol 2, p 582

12 Gruber, G. B. in von Lichtenberg, A., Voelcker, F., and Wildbolz, H. *Handbuch der Urologie*, Berlin Julius Springer, 1928, p 78

13 Delbet, P. *Ann d mal d org genito-urin* **25** 641, 1907

14 Orth, Johannes. *Lehrbuch der speciellen pathologischen Anatomie*, Berlin, A. Hirschwald, 1889, vol 2, p 201

15 Pagenstecher, E. *Arch f klin Chir* **74** 186, 1904

to the cause. With the thought in mind that the corrosive effect of serum electrolytes might be a factor, four tacks of each metal were immersed in 5 cc of Ringer's solution<sup>7</sup> for thirty days. The tubes were kept at 37.5 C and gently

TABLE 4—*Loss of Weight of Low Nickel Rustless Steel*

Pin	Dog	Bone	Weight of Tack, Gm		Percent age of Loss	Days in Bone	Comment
			Before Insertion	After Removal			
25	4	Tibia	0.313	0.313	0	75	Slight periosteal reaction
26	4	Tibia	0.313	0.310	0.95	75	Periosteal overgrowth
27	3	Tibia	0.311	0.307	1.10	40	Thin periosteal overgrowth
28	3	Tibia	0.307	0.304	0.81	40	Thin periosteal overgrowth
29	5	Tibia	0.300	0.297	1.00	75	Slight periosteal reaction
30	5	Tibia	0.295	0.291	1.30	75	Slight periosteal reaction
31*	4	Tibia	0.284	0.276	2.70	30	Slight periosteal reaction, partially extruded
32	4	Tibia	0.278	0.278	0	30	Periosteal overgrowth
33*	5	Femur	0.225	0.225	0	30	Extruded from the bone
34	5	Tibia	0.239	0.236	1.20	30	Slight periosteal reaction
35*	2	Tibia	0.274	0.268	2.07	30	Tack injured in removal
38	1	Femur	0.345	0.341	0.85	30	Periosteal overgrowth

\* Excluded from the final computation.

TABLE 5—*Loss of Weight in Ringer's Solution*

Pin	Weight of Tack, Gm		Percentage of Loss	Precipitate	Material
	Before Insertion	After Removal			
7	0.1902	0.1856	2.4	Heavy	Vanadium steel
8	0.1819	0.1761	3.2	Heavy	Vanadium steel
10	0.2037	0.1978	2.9	Heavy	Vanadium steel
11	0.2045	0.1920	2.7	Heavy	Vanadium steel
13	0.2487	0.2455	1.3	Heavy	Nickel free rustless steel
14	0.2405	0.2479	1.1	Heavy	Nickel free rustless steel
15	0.2442	0.2414	1.1	Heavy	Nickel free rustless steel
16	0.2643	0.2618	0.9	Heavy	Nickel free rustless steel
1	0.2239	0.2239	0	None	High nickel rustless steel
2	0.2447	0.2447	0	None	High nickel rustless steel
3	0.2264	0.2264	0	None	High nickel rustless steel
9	0.2244	0.2244	0	None	High nickel rustless steel
4	0.2821	0.2821	0	None	Low nickel rustless steel
5	0.2875	0.2875	0	None	Low nickel rustless steel
6	0.2625	0.2625	0	None	Low nickel rustless steel
12	0.3074	0.3074	0	None	Low nickel rustless steel

<sup>7</sup> The formula used for Ringer's solution is as follows. Each 10 cc contained 0.05 Gm of sodium chloride, 0.002 Gm of potassium chloride, and 0.004 Gm of calcium chloride.



in length, namely, that of the corpus vesicae and that of the trigonum" Kaufmann<sup>16</sup> stated that the division of the bladder into two chambers is a very rare finding and that the explanation of this developmental defect is difficult. Aschoff<sup>17</sup> did no more than mention the anomaly.

Chwalla,<sup>18</sup> as a result of researches on a 37 mm female embryo which he sectioned serially, found an interesting anomaly of the bladder, which was the only defect in the specimen. The bladder was markedly contracted. The mucosa about the ureteral orifices was arranged in folds. There was, in addition, a constriction of the lateral walls of the bladder. On sectioning the bladder, a membrane was found protruding into the cavity of the bladder, which was two or three cell layers thick and bound the anterior to the posterior wall. The membrane was thinner in the center and thicker toward the periphery. Similar to the constriction from side to side there was a moderate drawing in of the ventral wall of the bladder and a rather marked drawing in of the posterior wall. Chwalla interpreted this membrane as a persistent rest of the "ureter membrane," described by himself as a normal structure in embryos from 12 to 28 mm, which completely closes the openings of the ureters in embryos of this size but in embryos more than 28 mm in length becomes deliscent and disappears.

Paschkis and Krasa<sup>19</sup> had the opportunity of carefully studying the bladders of most of the animals from the zoological gardens in Vienna, and their monograph on the comparative anatomy of this organ is a classic. They found that in certain animals, especially in the monotreme, or duckbill, in the talpa, or mole, and in *Equus asinus*, a transversely divided bladder is the rule, and in a footnote they made the suggestion that this finding may have some bearing on the subject of transversely divided or hour-glass bladders seen in human beings.

We can obviously express no more than a theoretical opinion as to the cause of this rare anomaly based on what is at present known about the embryology of the bladder. First, we shall consider Krasa's and Paschkis' point of view, namely, that there exists a relationship between the divided bladders seen normally in certain lower animals and the very rare anomaly of hour-glass bladder in man. While the suggestion of an atavistic phenomenon is interesting and very plausible, it is a fact that in those animals which show the type of divided bladder noted

16 Kaufmann, E. *Lehrbuch der speziellen pathologischen Anatomie*, eds 7 and 8, Berlin, W. de Gruyter & Co., 1922, p. 1116.

17 Aschoff, L. *Pathologische Anatomie*, ed 4, Jena, Gustav Fischer, 1919, vol 2, p. 558.

18 Chwalla, R. O. *Zur Genese der angeborenen Sanduhrblase*, *Ztschr. f. urol. Chir.* 23 200, 1927.

19 Paschkis, R., and Krasa, F. C. *Ztschr. f. urol. Chir.* 6 1 (Jan.) 1921.

agitated once daily. The solution was changed every three days. That these electrolytes have a profound effect was clearly demonstrated as early as forty-eight hours after the beginning of this experiment. At the end of thirty days, corrosion was graphically illustrated by a heavy precipitate at the bottom of the test tubes. The changes in weight can be seen in table 5.

The reaction of the bone to the metal foreign body was studied. A thin segment of the bone containing the defect created by the tack was removed and fixed in a 10 per cent dilution of solution of formaldehyde U S P, and was then

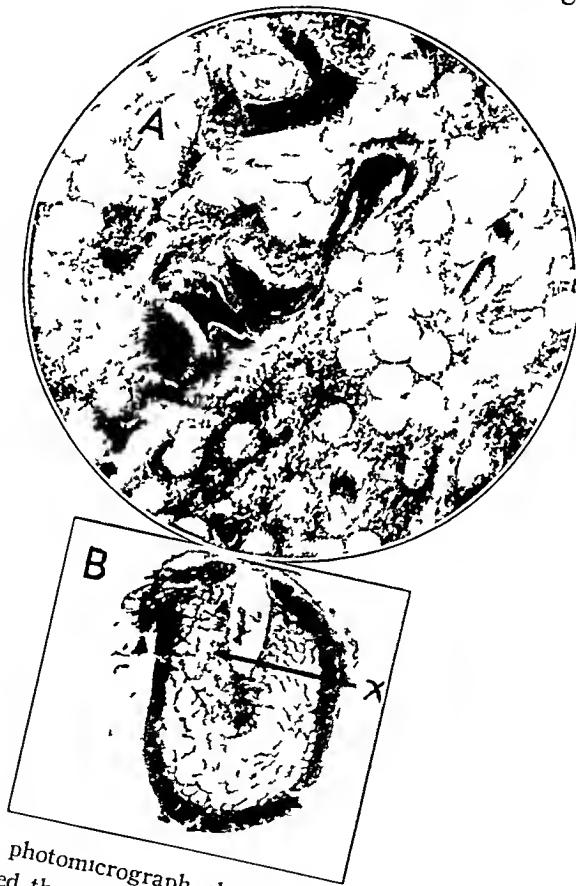


Fig 3—*A*, high power photomicrograph, showing reaction of bone to vanadium steel after the tack remained thirty days in the femur. *B*, low power photomicrograph, showing the extent of the zone of the medullary and periosteal reaction, indicating the site shown in *A*. This demonstrates the extensive character of the inflammatory change and bone resorption induced by vanadium steel.

decalcified, sectioned and stained with eosin and hematoxylin. No blocks were selected for study from bones containing more than a single tack or from bones in which the tacks were left longer than thirty days. The intensity of the reaction varied considerably, even when the same metal was used. However, each metal had certain definite characteristics.

the musculature of the ureter most perfectly merges with the musculature of the bladder, and therefore a comparison based on this embryonic characteristic does not seem entirely warranted

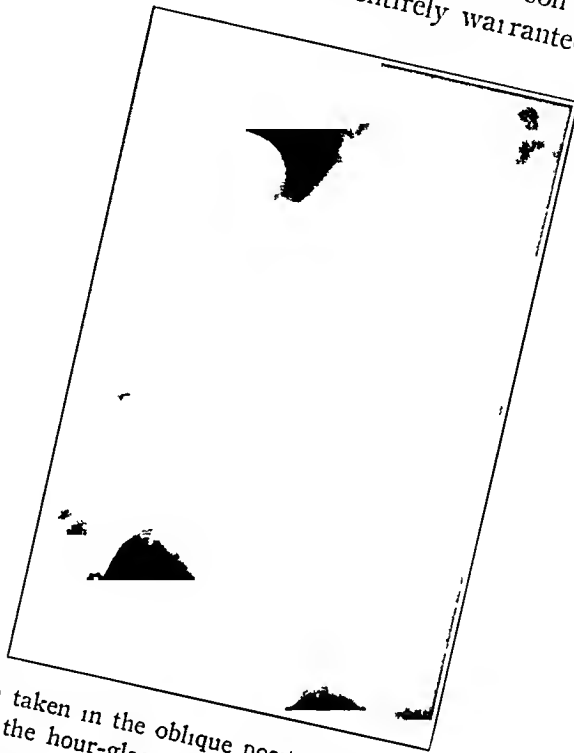


Fig 1—Cystogram taken in the oblique position. Note the diverticulum above the upper chamber of the hour-glass bladder



Fig 2—Anteroposterior view of the bladder shown in figure 1. Note the incidental reflux up the right ureter

In regard to Chwalla's<sup>18</sup> point of view, that the ledge on diaphragm may be a rest of the embryonic membrane of the ureter, it is to be said that, while it is conceded that Chwalla's description of the membrane closing the ureters in embryos of from 12 to 28 mm is correct,

Macroscopically, the sections of vanadium steel showed a wide zone of increased density extending into the marrow for a distance approximately the length of the tack. Microscopically, there was marked fibrous thickening of periosteum with recent inflammatory changes adjacent to the defect. The bone marrow showed a vastly increased cellular content around the wedge-shaped defect. The zone of reaction was double the width of the defect near the cortex, and at the apex of

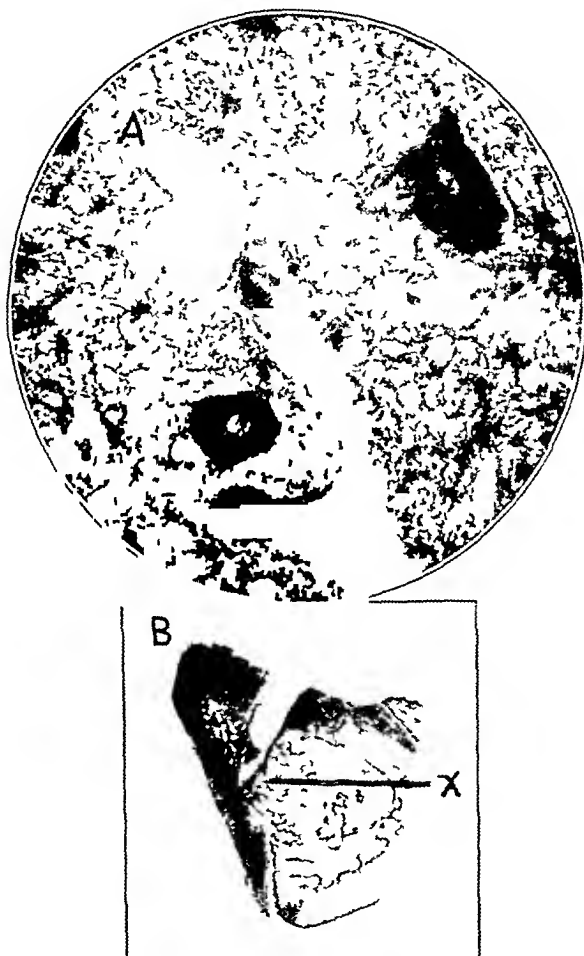


Fig 4—*A*, high power photomicrograph, showing reaction of bone to nickel-free rustless steel after the tack remained thirty days in the tibia. *B*, low power photomicrograph, showing defect created by the tack, and the extent of the zone of medullary reaction, *x* indicating the site shown in *A*. This demonstrates the resultant extensive hemorrhage, lymphocytic infiltration and necrosis of bone.

the wedge it extended almost to the opposite cortex. The cellular infiltrate was composed of lymphocytes and erythrocytes lying in greatly distended vessels or free in the marrow spaces. The erythrocytes predominated. The bone trabeculae proximal to the defect exhibited marked rarefaction by osteoclasts.

the conclusion based on a single finding of an anomaly in an embryo of 37 mm, that this defect is a test of the membrane of the ureter, is not wholly tenable. It has not been shown that this membrane shifts or changes its position rather than merely becoming dehiscient and disappearing as is the rule. If the constricting band or perforated diaphragm were always noted exactly at the site of the entrance of the ureteral orifices, as in Mezan's case, rather than above them, as in our case and in others of similar character, or below their entrance into the bladder, as reported by Fuller, Detweiler and Cutler, more weight could be given to his opinion.

It seems that the opinion expressed by Pagenstecher and by Gruber is correct, namely, that an unequal growth of the anlagen of the bladder would account for both types of hour-glass bladder, whether the ureters entered into the upper or into the lower chamber. To support this view

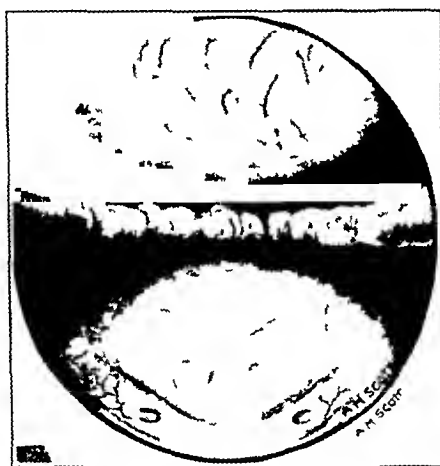


Fig. 3—Diagrammatic drawing of cystoscopic findings. Note the heavy muscular ledge dividing the bladder cavity into two compartments.

it is to be recalled that the portion of the bladder between the ureteral orifices and the colliculus is of mesodermal origin, while the bladder cavity itself is of endodermal origin. The anlage of the ureter is gradually taken up by the anlage of the bladder, and any failure of perfect coalescence of these two structures of different origin could produce transverse folds or fibromuscular ledges either above or below the entrance of the ureters into the bladder.

#### PATHOLOGY

The pathology of true hour-glass bladder must be divided into a study of the separating membrane or diaphragm and of the pathologic physiology resulting from the anomaly. In none of the reports have we found any reference to the tissue removed at operation or to examination of the tissue post mortem. Our specimen was grossly a thick

The gross reaction to nickel-free rustless steel varied from that to vanadium steel in degree only in that it was not quite as extensive. Microscopically, there were intense hyperemia and dense cellular infiltration of the bone marrow throughout the section. The prevailing cells were erythrocytes, with the lymphocytes represented in lesser number. Trabeculae lined the defect directly, and all those adjacent showed marked rarefaction by osteoclasia.

Grossly, the reaction to high nickel rustless steel presented a small zone of change. There was only slight periosteal overgrowth. Microscopically, the defect was lined by smooth bone surface or exposed trabeculae and bone marrow spaces.

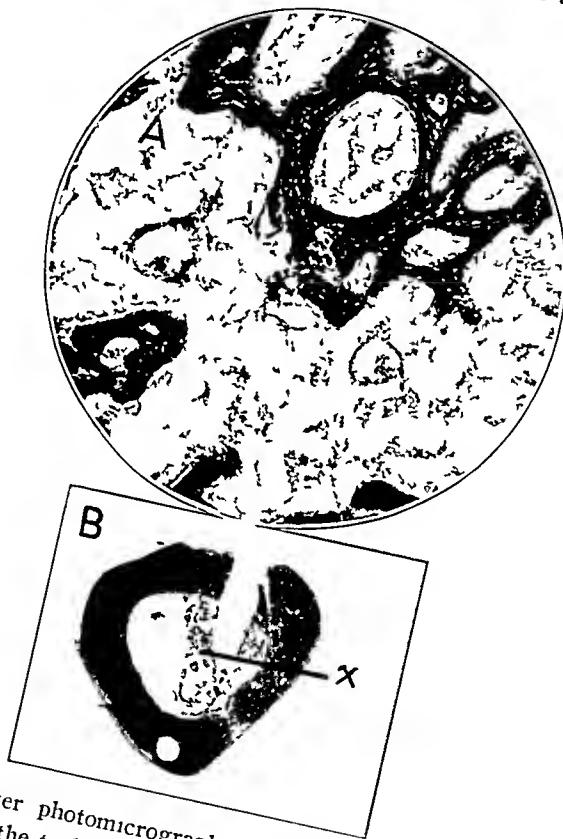


Fig 5—*A*, high power photomicrograph, showing reaction of bone to high nickel rustless steel after the tack remained thirty days in the tibia. *B*, low power photomicrograph, showing a narrowed zone of medullary reaction, *x* marking the site shown in *A*. Here is seen the greatly diminished inflammatory reaction, as compared with that seen in the two preceding figures. There are retention of trabecular structure and minimal resorption of bone.

without the formation of a definite fibrous tissue layer over considerable areas. There was moderate fibrosis in the medulla close to the margin. Hyperemia in this zone was marked, with scattered hemorrhages and cellular infiltration. The entire bone marrow in this section showed a similar condition. Osteoclasia was slight and was limited to the trabeculae adjacent to the defect.

muscular and fibrous structure varying from 1 to 1.75 cm in thickness, completely crossing the posterior wall of the bladder and having its origin and insertion on the lateral walls well toward the ventral aspect of the bladder. In general it had the characteristics of tremendously hypertrophic bladder musculature which had undergone subsequent chronic inflammatory infiltration. Histologically, the picture was as follows. The section revealed an apparent increase of connective tissue throughout. In addition a few lymphocytic cells and endothelial cells were noted, some of which were perivascular in distribution. Sections

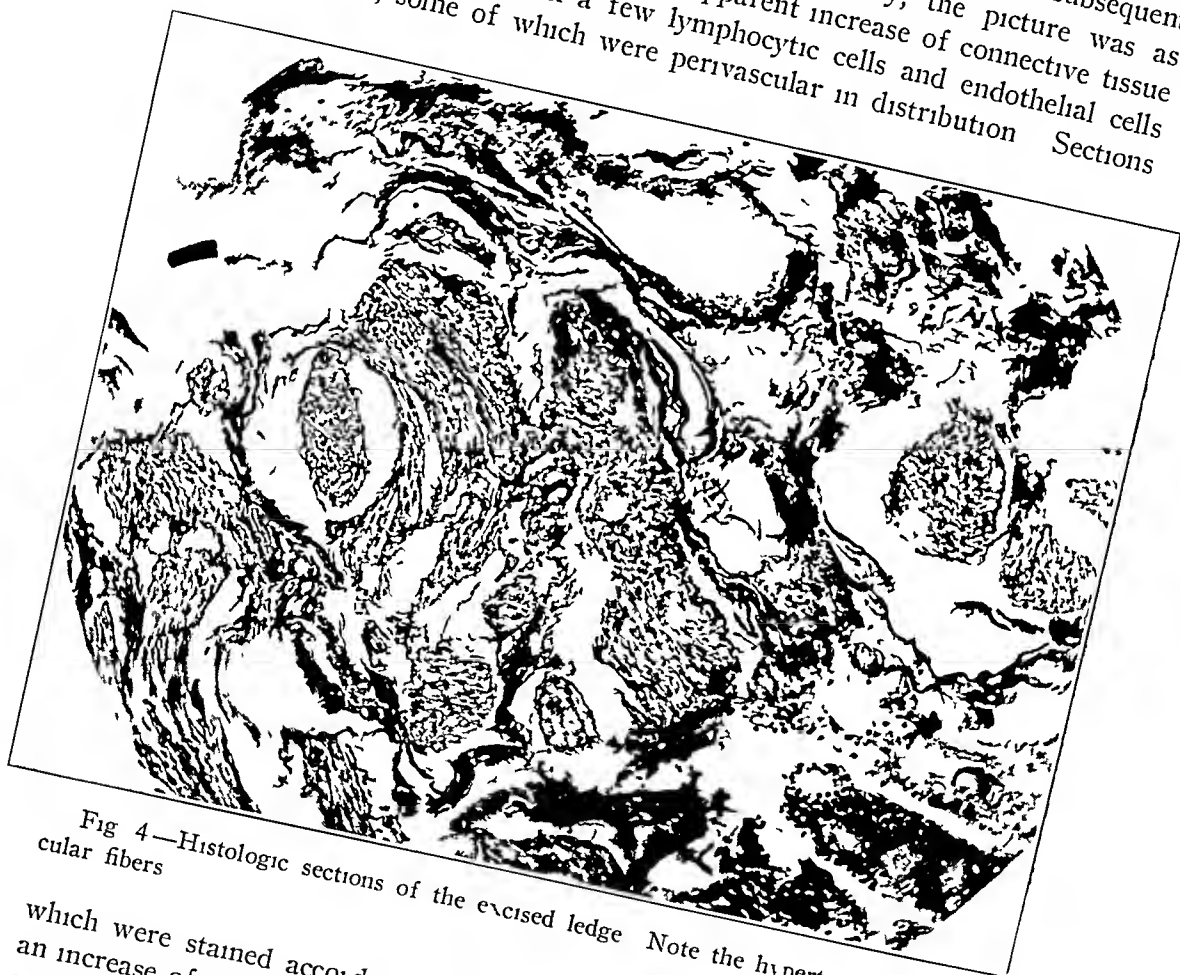


Fig 4—Histologic sections of the excised ledge. Note the hypertrophic muscular fibers.

which were stained according to the Van Gieson method also showed an increase of connective tissue. The muscle fibers and muscle bundles seemed somewhat larger than normal, otherwise no changes were noted.

#### PATHOLOGIC PHYSIOLOGY

The pathologic physiology of hour-glass bladder seems not too difficult of interpretation and depends largely on the character and contour of the constricting band. As a result of the presence of a prominent ledge or perforated diaphragm, the normal contractions of the detrusor muscle are inhibited from time to time, causing failure of the

the various groups, the death rate from simple acute appendicitis remains at a fairly constant low level. The mortality from acute appendicitis with acute local peritonitis has shown a distinct decline. On the other hand, the mortality rate has increased in the next two groups, cases of acute appendicitis with abscess and of acute appendicitis with acute diffuse peritonitis. To be sure, the recent annual death rate in both groups shows a distinct decline, but the five year average leaves no doubt as to its increase compared to former periods. The death rate from acute appendicitis with acute fibrinopurulent peritonitis remains consistently high, but this should not discourage one from enlisting one's greatest efforts in an attempt to save patients with this condition. The very fact that 3 actually did survive should encourage one to carry on a strong battle for their lives.

Discussions on the possible means of reducing the mortality in the various groups (except group 4, acute appendicitis with acute diffuse peritonitis, which will appear in a separate paper) have already been given, and they need not be repeated here. They may merit consideration on the part of the surgeon who is ever anxious to better his results.

There should be perfect team-work on the part of the hospital staff in the treatment of patients with peritonitis and abscess. The older experienced men should guide and direct the younger attending surgeons and house staff officers in handling these cases, because they demand the most careful, balanced and mature judgment, the problems and complications may be extremely difficult to comprehend and to combat.

One phase in the possible reduction of the mortality rate does deserve discussion here, namely the problem of prevention. This directly concerns the laity as well as the medical profession and is largely a public health problem. A cursory glance at the tables will show at once that the mortality rate in cases of simple acute appendicitis is very low, but as soon as perforation takes place with spreading peritonitis, the mortality rate is high. The public should learn that the early diagnosis of acute appendicitis followed by early operation by a competent surgeon at a well equipped hospital is attended by an extremely low mortality rate. There are certain factors which may interfere with this.

1. Certain fears and superstitions still exist in the minds of many that to enter a hospital and undergo an operation is an acknowledgment of defeat and can result only in certain death. The problem is often exasperating, and the practitioner can do nothing but observe the chances of recovery gradually diminishing with the advance of time. When consent to operation is finally given it may be too late.



2 Mothers still give their children cathartics for abdominal cramps and pains. The public health service and pediatricians should carry on a vigorous campaign against the indiscriminate use of such medicine. It is simpler and safer to give an enema instead or, at least, to give a cathartic only after examination by a physician.

3 The indiscriminate dispensing of purgatives and laxatives by the pharmacist is a factor. Persons constantly enter a drug store and request some medicine, to be recommended by the druggist, for abdominal pain. This practice is becoming increasingly widespread, especially in recent years when many persons have been unable to consult a physician.

4 Most persons associate appendicitis with pain on the right side. Few, if any, realize that an acute attack starts, as a rule, with generalized (or epigastric or periumbilical) abdominal cramplike pain. Consequently they believe they have an "upset stomach" or "indigestion," and resort to the time-honored cathartic. Only later, when the pain localizes in the right side (and this does not always happen), do they call a physician. Meanwhile, valuable time has been lost. It is most important to educate the public, therefore, that pain on the right side develops only later in cases of acute appendicitis, and they should learn to appreciate the factor of delay in its relation to mortality.

5 The physician himself may be unable to recognize some of the early atypical cases of acute appendicitis. If that is the case he should observe the patient frequently, perhaps every two hours, until more definite signs develop. He should remember never to give opiates for abdominal pain until he can make a definite diagnosis. In the event of continued doubt he should always request a consultation even though it may touch his pride a bit, surely a doctor's pride cannot compare with a patient's life. He must learn to regard with suspicion any abdominal pain that persists over six hours.

6 The practitioner knows only too well that a certain number of cases of acute appendicitis will subside with morphine, rest and the use of an ice bag. He institutes this therapy for twenty-four hours (the most important factor in reducing the mortality is therefore lost) and returns the next day. If the patient is better, the therapy is continued and recovery probably takes place. The physician is considered a miracle man, he saved his patient from an operation and "froze" out the appendix. But what if the patient is worse or only about the same? The physician will decide to send him to the hospital or else will determine to watch him for another twenty-four hours. In either case the damage has been done. The patient no longer has a localizing process, but probably spreading peritonitis, due to perforation or gangrene of the appendix. The physician has done "his best," he

upper chamber to empty itself completely. Owing to stasis in the upper chamber of the divided bladder, infection is invited at an earlier or later period in the patient's life. Bacteria, once having gained access to the bladder, persist indefinitely as they do in bladders subjected to other obstructive processes.

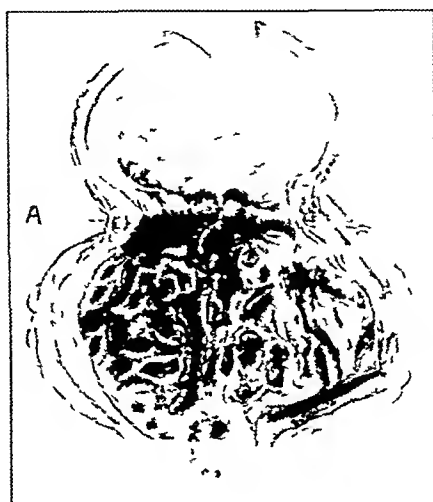


Fig 5—Drawing of the bladder in the case of Kretschmer and Morris<sup>2</sup> (courtesy of the *Journal of Urology*). A indicates the definite firm constriction which divides the bladder into two cavities.

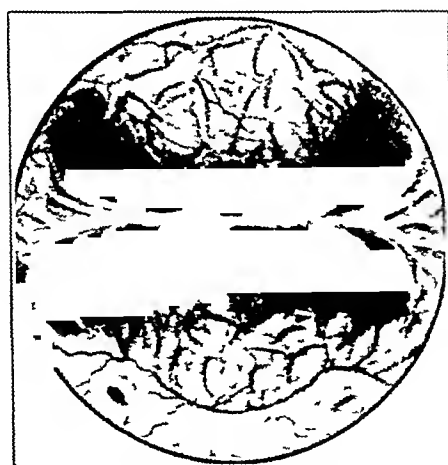


Fig 6—Drawing of the bladder in Caulk's<sup>3</sup> case (courtesy of the *Annals of Surgery*).

Vesical spasm, evidenced by frequent and painful urination, occurs and the bladder as a whole or in part contracts more often on account of the irritability produced by inflammation. The increased mechanical work of the bladder musculature causes hypertrophy of its wall as a whole, more particularly in the immediate neighborhood of the con-

acid-secreting cells of the stomach during fasting. It has been so used in the rat (Buchner<sup>39</sup> and Molloy<sup>40</sup> and Siebert,<sup>41</sup> Burkle-de la Camp<sup>42</sup>), in the mouse (Harde<sup>43</sup>), in the cat (McIlroy,<sup>44</sup> O'Shaughnessy<sup>45</sup>), in the rabbit (Matsueda<sup>46</sup>), in the guinea-pig (Harde, Matsueda) and in the dog (Matsueda, Puhl and Brodersen,<sup>47</sup> Friedenwald, Feldman and Morrison). The gastric juice secreted as a result of adequate doses of histamine is capable of producing peptic injury in the mucosa of the stomach, showing all transitions of mucosal changes from erosion to acute and chronic ulcers, this depending on whether or not the animal is fasting.

Since Meckel<sup>48</sup> first described his diverticulum in 1815, more and more interest is being shown in this condition because of the dramatic clinical picture of ulceration, hemorrhage and perforation which the functionally active dystopic gastric mucosa when present in Meckel's diverticulum is wont to produce through its acid peptic secretion. These ectopic tissues, the heteromorphoses of the biologists and the heteroplasias of the pathologists, have long held the keen attention of investigators, as judged from the extensive literature on the subject (Nicholson,<sup>49</sup> Taylor<sup>50</sup>). All these congenital heterotopias, whether of the gastric gland or of the intestinal gland type, are explainable perhaps by the ontogenetic history of the patient, they are the expression of his dysontogenesis. Such congenital heterotopias of various types occur in different portions of the gastro-intestinal tract. Recently, Mondor and Lamy<sup>51</sup> collected reports of nearly one hundred cases of ulcer of Meckel's diverticulum. A similar condition exists after the performance of a gastro-enterostomy, when jejunal mucosa becomes bathed with the acid secretions of the stomach, ulceration often resulting. When an isolated loop of small intestine is used to form a fistulous

39 Buchner, F, and Knotzke, F. Beitr z path Anat u z allg Path **80** 496, 1928

40 Buchner, F, and Molloy, P J. Klin Wchnschr **6** 2193, 1927

41 Buchner, F, Siebert, P, and Molloy, P J. Beitr z path Anat u z allg Path **81** 391, 1928

42 Burkle-de la Camp, H. Deutsche Ztschr f Chir **220** 31, 1929

43 Harde, E. Compt rend Soc de biol **109** 1326, 1932

44 McIlroy, P T. Proc Soc Exper Biol & Med **25** 268, 1927

45 O'Shaughnessy, L. Lancet **1** 177, 1931

46 Matsueda, A. Klin Wchnschr **10** 2265, 1931

47 Puhl, H, and Brodersen, H. Arch f klin Chir **168** 31, 1931

48 Meckel, J F. Arch f d ges Physiol **1** 293, 1815

49 Nicholson, G W. Guy's Hosp Rep **71** 222, 1921, **72** 193, 333 and 402, 1922, **73** 37, 164 and 298, 1923, **74** 81, 1924

50 Taylor, A L. J Path & Bact **30** 415, 1927

51 Mondor, H, and Lamy, M. J de chir **41** 553 1933

stricting band. Thus a vicious circle is produced, which, as the pathologic process advances, causes increased thickening of the band with subsequent narrowing and more marked retention in the proximal or upper chamber. Obviously, if infection remains absent till after middle life or if obstructive processes at or near the neck of the bladder do

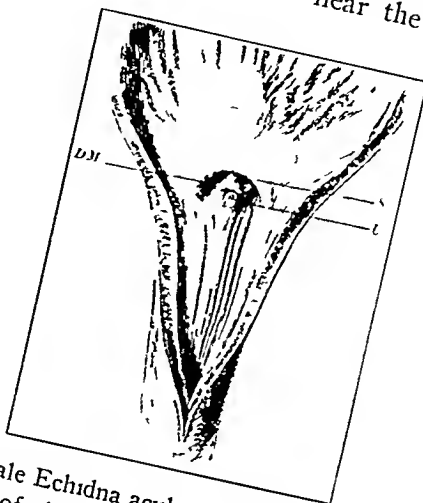


Fig 7—Bladder of female *Echidna aculeata* (courtesy of Paschkis and Krasa<sup>19</sup>)  
*DM* indicates the position of the ductus Mulleri, *S*, shows the sphincter, and *U*, the opening of the ureter

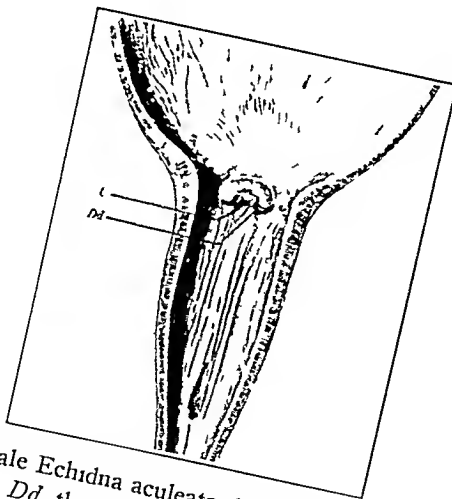


Fig 8—Bladder of male *Echidna aculeata* (courtesy of Paschkis and Krasa<sup>19</sup>)  
*U* indicates the ureter, and *Dd*, the ductus deferens

not occur, the hour-glass bladder of this type may function in a relatively normal manner. The degree of development of the ledge or perforated diaphragm will determine the onset of conspicuous evidence of dysfunction. For example, if the communication between the two chambers is wide, retention in the upper chamber will be minimal, while if this communicating opening is narrow, the converse will be true. The condition tends to

tract for the stomach (Goldberg,<sup>52</sup> Harper<sup>53</sup>), a chronic peptic ulcer develops in the mucosa of this fistula, just distal to the suture line between it and the stomach. Matthews and Dragstedt<sup>54</sup> reproduced Meckel's diverticulum with heterotopia by making a small Pavlov pouch which emptied into the isolated loop of the lower portion of the ileum. When the gastric pouch, with or without nerves, was implanted into the ileum, the incidence of ulcer was 100 per cent, but it was only 85 per cent when the pouch was implanted into the jejunum.

#### PROCEDURE

The present investigation<sup>55</sup> was undertaken in an attempt to evaluate the etiologic importance of gastric acidity. The effects of increased gastric acidity obtained by feeding hydrochloric acid and by stimulation with histamine were determined. Subsequently the incidence of peptic ulceration was determined in animals in which gastric pouches from the greater and lesser curvatures of the stomach, respectively, were anastomosed with the jejunum. Normal healthy dogs were used in all experiments. Every animal was weighed. The range of normal gastric acidity (free, combined and total) was first determined from two to five different times at intervals of from four or five days to a week following a standard test meal consisting of 22 Gm of cracker meal in 250 cc of water given through a stomach tube after fasting. When the following series of experiments was started the animals fasted on alternate days, at which time either the feeding of hydrochloric acid or injections of histamine were given and gastric analysis was carried out. Histamine acid phosphate was used. The solution was prepared by weighing the chemical under sterile conditions and dissolving it in sterile distilled water. In none of the animals did an abscess develop at the site of the injections. For the determination of gastric acidity, the technique as described in Bass and Johns' "Practical Clinical Laboratory Diagnosis"<sup>56</sup> was followed, di-methylamino-azobenzene and phenolphthalein being used as indicators. Computation gave values for free hydrochloric acid and total acidity. The difference between them represented the value for combined hydrochloric acid. The presence of bile and mucus was noted in each specimen obtained through the stomach tube.

A total of 125 dogs was used, but of this number 69 died at various intervals after operation, leaving 56 animals on which our results are based. These experiments extended over a period of over three years. The postoperative mortality in the 69 animals not used for analysis in the present series was attributable in a great measure to postoperative peritonitis and surgical shock, a few deaths were due to an overdose of ether (2 animals) or distemper (9 animals). In the surviving dogs, death was generally due to a more or less general debilitated condition.

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52 Goldberg, S. L. Intrinsic Regulation of Gastric Acidity, *Arch Int Med* **49** 816 (May) 1932, *Ann Surg* **96** 155, 1932.

53 Harper, F. R. *Proc Staff Meet, Mayo Clin* **7** 318, 1932.

54 Matthews, W. B., and Dragstedt, L. R. *Surg, Gynec & Obst* **55** 265, 1932.

55 A preliminary report was published in 1934 (Ochsner, A., Gage, M., and Hosoi, K. *Proc Soc Exper Biol & Med* **31** 1260, 1934).

56 Bass, C. C., and Johns, F. M. *Practical Clinical Laboratory Diagnosis*, Baltimore, Williams & Wilkins Company, 1929, chap 9, p 104.

become very slowly progressive but is rather promptly affected by any pathologic process involving the neighborhood of the neck of the bladder or structures distal to it, such as stricture of the urethra, prostatovesiculitis, prostatic hypertrophy or contracture of the neck of the bladder

#### SYMPTOMS

The symptoms of true hour-glass bladder are variable, and in no particular are they pathognomonic of the condition. In some cases

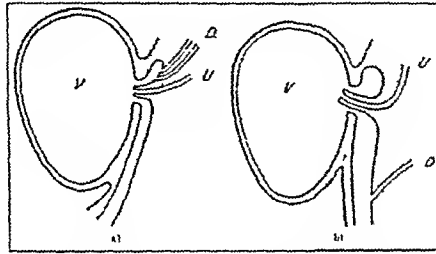


Fig 9—Sagittal view of bladder (A) Echidna, (B) Didelphys (courtesy of Paschke and Krasa<sup>19</sup>)



Fig 10—Anteroposterior view of the bladder fifteen months after operation

urinary dysfunction had been present from childhood or early youth, as evidenced by enuresis and frequent and painful micturition. In other cases no symptoms of consequence evidenced themselves until middle age or later, when pathologic conditions having no connection with the congenital anomaly elicited symptoms of greater severity and degree than would have been occasioned by the pathologic process present, if uncomplicated. Pagenstecher remarked that clinical symptoms usually appear first when the constriction becomes so marked that the emptying of the upper chamber is greatly interfered with. Our patient presented the characteristics noted and undoubtedly had an exaggeration of the comparatively mild symptoms of his childhood and youth as a result

induced by repeated feedings of hydrochloric acid, injections of histamine or peptic ulceration. Perforation of an acute or chronic ulcer into the peritoneal or pleural cavity was the cause of sudden death in 10 dogs (peritoneal perforation in 9 and pleural perforation in 1). The animals were generally killed when they were much debilitated instead of waiting for them to die. They were kept in separate cages, which were cleaned daily. Fresh drip water was a constant source of water supply. On clear sunshine days the animals were taken out on the roof to bask freely in the sun for several hours. From this it will be seen that poor environmental conditions cannot be said to be of etiologic importance in our experiments.

Necropsy was performed soon after death. Specimens were removed and immediately fixed in 10 per cent neutral solution of formaldehyde or Zenker's fixative. The hematoxylin and eosin stain was used for general cytologic study and Mallory's aniline blue stain was used for evidence of increased fibrosis as the result of the ulceration. All the lesions described in our experiments were submitted to microscopic study for verification as to whether they were mucosal hemorrhages, erosions or acute or chronic ulcers. Also for purposes of comparative study to serve as controls, sections were obtained from the gastro-intestinal tracts of presumably healthy dogs which had been electrocuted.

All animals except the controls received thrice daily every other day either a feeding of hydrochloric acid or an injection of from 0.25 to 0.8 mg. of histamine subcutaneously. Four experiments were performed as follows: experiment 1, in which no surgical procedure was done to determine the gastric reaction to feeding of hydrochloric acid and injections of histamine, experiment 2, extirpation of (a) the greater curvature (fig. 1a) and (b) the lesser curvature (fig. 2), experiment 3, formation of a gastric pouch from (a) the greater curvature (Heidenhain type, fig. 1b) or (b) the lesser curvature (Pavlov type) plus anastomosis of the proximal jejunum to the pouches (fig. 3), and experiment 4, the same as experiment 3 plus anastomosis of the fundus of the gallbladder to the pouches (figs. 4 and 5). In experiments 2, 3 and 4 control animals were used, which were not given hydrochloric acid or histamine but in which the respective operations were performed. Repeated gastric analyses were carried out preoperatively and postoperatively on all animals.

Postoperatively, irrespective of the character of the operation, the following routine was used. Immediately after the operation an intravenous infusion of a warmed 5 per cent solution of dextrose in normal lactate-Ringer solution was given into the external jugular vein about 50 cc. per kilogram of body weight. For the next three days an infusion was given once daily of the same amount of dextrose in lactate-Ringer solution. The animal was allowed nothing by mouth, not even water, during this period. From the fourth to the sixth postoperative day inclusive, the dogs were fed twice daily equal parts of Karo corn syrup and milk and were allowed to drink water. Only rarely did they vomit this milk mixture. The animals that appeared weak, especially after the more prolonged types of operation, were given another three day course of feeding of Karo syrup and milk. Usually on the seventh postoperative day they were returned to the normal stock kennel chow diet of one feeding a day.

**EXPERIMENT 1**—*Observations on dogs in which no surgical procedure was carried out, to obtain the gastric reaction to repeated feedings of 1 per cent hydrochloric acid (8 dogs) or injections of histamine (7 dogs).*

Repeated feedings of 1 per cent hydrochloric acid to 6 or 8 fasting dogs produced acute lesions consisting of petechiae, erosions and shallow ulcers in both

of the interference with urinary outflow. The presence of changes in the neighborhood of the neck of the bladder unquestionably had considerable bearing on the inflammatory as well as on the mechanical pathologic elements in the clinical picture, as observed before operation.

## REPORT OF A CASE

*Present Complaint*—O. B., aged 42, was admitted to the hospital because of urinary frequency, dysuria, nocturia (he arose five or six times a night) and pain in the region of the bladder.

*History*—The patient stated that he suffered from enuresis until he was 14 years of age, at which time this condition ceased. No other illnesses of consequence were mentioned in the anamnesis. He said that he had not had venereal



Fig. 11—Lateral view of the bladder shown in figure 10, fifteen months after operation.

disease. In 1918 he had influenzal pneumonia. During his convalescence he noticed some dysuria, which had gradually become worse until the time of admission. He stated that the dysuria became aggravated when he "caught cold." In 1925 the dysuria, frequency and pain in the region of the bladder were so severe that he was required to undergo a cystoscopic examination, which was done elsewhere. After cystoscopy he had complete retention of urine owing to the presence of blood clots in the bladder. A cystotomy was then done, an inlying urethral catheter was tied in, and the opening was permitted to close after five weeks. The symptoms continued the same, and he went to a clinic in the Northwest, where a diagnosis of moderate pyelitis, chronic prostatitis and posterior urethritis was made.

*Physical Examination*—The results of general external examination were negative except for definite and marked suprapubic tenderness. The results of the various examinations were as follows:



the stomach and the duodenum. These acute lesions were present as early as five and eight days after the administration of 1 per cent hydrochloric acid three times daily on alternate days in 2 dogs, respectively. The lesions were usually multiple. Feeding of hydrochloric acid for eight days produced three acute lesions of the stomach and duodenum, proved microscopically, in only 1 of these dogs.

TABLE 1—*Incidence of Ulcers in Animals Following Feeding with Hydrochloric Acid*

Dog	Date	Acidity Before Administration of 1% Hydrochloric Acid			Acidity After Administration of 1% Hydrochloric Acid Began			Dura- tion, Days	Ulcer	
		Hydrochloric Acid			Hydrochloric Acid					
		Free	Com- bined	Total	Date	Free	Com- bined			Total
HH 1	1/13/32	36	24	60	1/21/32	30	23	53	55	Yes Erosions
	1/15/32	28	32	60	1/22/32	36	15	51		
	1/16/32	57	21	78	1/23/32	20	9	29*		
					1/29/32	28	16	44*		
					2/ 4/32	42	18	60*		
					2/ 5/32	39	14	53		
					2/15/32	47	17	64		
					2/19/32	45	15	60*		
					2/25/32	52	40	92		
					3/ 4/32	53	45	98		
					3/10/32	35	29	64		
HH 2	12/23/31	18	10	28	1/21/32	25	18	43	25	No
	1/ 5/32	46	17	63	1/22/32	30	17	47		
	1/ 7/32	35	19	54	1/23/32	37	18	55		
	1/11/32	37	19	56	1/29/32	32	28	60		
	1/12/32	33	6	39	2/ 4/32	26	19	45*		
					2/ 5/32	23	18	41		
HH 3	1/22/32	33	25	58	2/ 4/32	0	21	21	26	Erosions
					2/ 5/32	0	13	13		
HH 23	2/12/32	38	4	42	2/25/32	0	10	10	13	Petechiae
	2/15/32	58	26	84						
	2/18/32	25	10	35						
	2/19/32	31	10	41*						
HH 31	3/ 4/32	15	15	30	3/24/32	0	5	5*	5	Erosion hemorrhage
	3/10/32	18	4	22						
	3/17/32	9	9	18						
	3/21/32	18	39	57						
HH 32	3/10/32	0	10	10	3/24/32	0	5	5	8	Ulcers of pylorus and duodenum
	3/17/32	15	14	29						
	3/21/32	0	14	14						
HH 41	4/ 1/32	13	5	18	4/ 7/32	0	8	8	13	Erosions of stomach and duodenum
	4/ 4/32	22	10	32	4/15/32	0	8	8*		
					4/21/32	0	9	9*		
HH 42	4/ 1/32	4	4	8	4/ 7/32	21	17	38	13	No
					4/15/32	0	8	8		
					4/21/32	0	23	23		

\* Bile

Although the longest period of experimentation was fifty-five days for this group, ulcers were not obtained in other dogs. Microscopically the mucous cells everywhere in the different sections appeared prominent, with their cell bodies swollen, with a large mucoid globlet pushing the nucleus of the cell to one side and flattening it. This activity of the mucous cells of the stomach to greater production of mucus

**Rectal Examination** Rectal examination revealed a prostate gland which was slightly enlarged, unevenly indurated and markedly tender. There were a moderate number of pus cells in the expressed fluid. The seminal vesicles were palpable, soft and very sensitive. The urine on repeated examination showed many pus cells and red blood cells.

**Cystoscopic Examination** A no. 21 Brown-Buerger cystoscope passed with slight difficulty. The contents of the bladder were turbid. The bladder vault was moderately hyperemic. An opening of a small diverticulum at the dome was visualized. The trigonum was edematous and reddened. Both ureteral orifices were slitlike and contracted rhythmically. What appeared at first to be the opening of a diverticulum was noted about  $1\frac{1}{2}$  inches (3.7 cm) above the upper margin of the trigon. This was shown later to be a transverse ledge extending across the posterior and lateral walls of the bladder, having its origin and insertion well toward the ventral wall of the viscus. The ledge was thick and appeared as a markedly hypertrophic musculature. A no. 6 catheter failed to pass up the ureter on either side at the first attempt but was eventually passed after no. 5 bougies had previously been passed on both sides. Cultures of the urine from the pelvis of the right kidney yielded streptococci. The pyelograms showed no abnormality other than a slight blunting of the calices of the right kidney.

**Urethroscopic Examination** Urethroscopic examination revealed an enlarged verumontanum with prominent sulci on each side. On the left side was an opening into a pocket or sac which undermined the trigon for about 2 cm. The opening was slightly irregular, and at the time of examination it was impossible to state whether the pocket seen might have resulted from trauma at the time of cystoscopy in 1925 or whether it was a congenital anomaly.

**Cystogram** The cystogram, especially in the lateral view, showed an hour-glass outline. The upper chamber was somewhat larger than the lower chamber. There was a marked indrawing of the ventral as well as of the dorsal wall of the bladder. A similar constriction was noted from side to side in the cystogram made from an anteroposterior view. The anterior wall was irregular in outline, and on the posterior wall above the constriction there were several small cclules. At the dome a moderate-sized diverticulum was noted.

**Operation**—With the patient under spinal anesthesia, after excision of the scar in the skin left by the cystotomy, the bladder was exposed in the usual manner. The peritoneal fold was detached by dissection with the fingers, with slight difficulty, up to the vertex, and the urachus was severed. The small diverticulum at the dome was resected extravesically, and repair of the defect was made in the usual manner. On exploring the interior of the open bladder, the wall of which was very markedly thickened, especially above the partial diaphragm noted on cystoscopic examination, the constricting band was seen and was found to be from 1 to 1.75 cm in thickness. The greatest thickness was at its junction with the wall of the bladder. It appeared as a somewhat irregular band of hypertrophic muscle fibers. It was seen to divide the bladder into two chambers with a communicating opening, which would approximately admit the tips of three fingers. The entire muscular band was excised and the defect was sutured. The bladder was closed about a Pezzar catheter, which was left in the upper angle of the opening made by cystotomy.

**Operation for Resection of the Neck of the Bladder**—Approximately three months after the removal of the constricting ledge, the Pezzar catheter having been left in place, the bladder was again opened, and with the electric cutting

TABLE 2—Incidence of Ulcers in Animals Following the Administration of Histamine Subcutaneously

Dog	Acidity Before Injections of Histamine			Acidity After Injections of Histamine Began			Dura- tion, Days	Ulcer		
	Date	Hydrochloric Acid		Date	Hydrochloric Acid					
		Free	Com- bined		Free	Com- bined			Total	
HH 4	12/32/31	33	28	61	1/21/32	37	23	60	155	No gastritis
	1/ 5/32	21	11	32	1/22/32	5	10	15		
	1/ 7/32	20	6	26	1/28/32	18	3	21		
	1/11/32	8	3	11	1/29/32	38	16	54		
	1/12/32	32	8	40	2/ 4/32	43	23	66		
					2/ 5/32	16	8	24		
					2/15/32	18	15	33		
	Received histamine				2/19/32	40	17	57		
	1/13 to 2/ 2/32, 0.04 mg per Kg daily				2/25/32	82	22	104		
	2/ 3 to 2/19/32, 0.08 mg per Kg daily				3/ 4/32	24	9	33		
	2/20 to 3/22/32, 0.6 mg per Kg every 2 days				3/10/32	32	11	43		
	3/24 to 6/16/32, 0.8 mg per Kg every 2 days				3/18/32	22	11	33		
					3/24/32	45	5	50		
					4/ 1/32	47	11	58		
					4/ 7/32	35	9	44		
					4/15/32	52	15	67		
					4/21/32	39	12	51		
					4/29/32	35	34	69		
					5/ 5/32	60	18	78		
					5/11/32	33	11	44		
					5/19/32	49	19	68		
					5/27/32	38	14	52		
					6/ 2/32	55	23	78		
					6/10/32	23	10	33		
HH 5	12/23/31	46	16	62	1/21/32	0	27	27	55	Hemorrhages
	1/ 5/32	27	17	44	1/22/32	25	21	46		
	1/ 7/32	25	13	38	1/28/32	33	32	65		
	1/11/32	71	64	135	1/29/32	28	30	58		
	1/12/32	29	9	38	2/ 4/32	35	45	78		
	Received histamine				2/ 5/32	32	28	60		
	1/13 to 2/ 2/32, 0.04 mg per Kg daily				2/15/32	10	15	25		
	2/ 3 to 2/19/32, 0.08 mg per Kg daily				2/19/32	30	10	40		
	2/21 to 3/ 4/32, 0.6 mg per Kg every 2 days				2/25/32	55	22	77		
					3/ 4/32	41	10	51		
HH 6	12/23/31	0	31	31	1/21/32	60	15	75	28	Gastritis
	1/ 5/32	43	20	63	1/22/32	35	11	46		
	1/ 7/32	52	12	64	1/28/32	26	5	31		
	1/11/32	5	8	13	1/29/32	65	17	82		
	1/12/32	28	15	43						
	Received histamine									
	1/13 to 2/9/32, 0.04 mg per Kg daily									
HH 25	2/12/32	30	19	49	2/25/32	35	15	50	14	Ulcers gastritis
	2/15/32	23	19	42	3/ 4/32	22	16	38		
	2/18/32	35	11	46						
	2/19/32	42	20	62						
	Received histamine									
	0.6 mg per Kg every 2 days									
HH 33	3/10/32	20	14	34	3/24/32	21	9	30	7	Petechiae, ulcers of stomach and duodenum gastritis duodenitis
	3/17/32	22	16	38						
	3/21/32	0	11	11						
	Received histamine									
	0.6 mg per Kg every 2 days									
HH 36	3/17/32	0	19	19	3/24/32	72	12	84	27	Hemorrhages erosions gastritis
	3/21/32	19	16	35						
	Received histamine									
	0.8 mg per Kg every 2 days									
HH 43	4/ 1/32	13	10	23	4/ 7/32	33	12	45	134	Ulcers hemorrhages gastritis
	4/ 4/32	34	26	60	4/17/32	35	10	45		
					4/21/32	43	11	54		
					4/29/32	53	10	63		
					5/ 5/32	41	18	59		
					5/11/32	51	11	62		
					5/19/32	53	10	63		
					5/27/32	37	11	48		
					6/ 2/32	38	13	51		
					6/10/32	45	15	60		
					6/16/32	55	22	77		
					6/24/32	12	76	88		
					6/30/32	35	35	70		
					7/ 8/32	19	16	35		
					7/14/32	24	41	65		
					7/22/32	10	23	33		
					7/28/32	20	22	42		
					8/ 5/32	23	15	38		
					8/11/32	21	19	40		
					8/19/32	51	22	73		

current a large V-shaped wedge was removed from the lower half and the neck. After two weeks the Pezzar catheter was removed, and the bladder was permitted to close.

The patient was able to urinate readily, and there was no residual urine. Cystograms taken twelve months after the resection of the neck of the bladder showed a remarkable change, and the appearance closely approached the normal outline of the bladder both in the anteroposterior view and in the lateral or oblique position.

#### COMMENT

*Diagnosis*—The direct diagnosis of true hour-glass bladder is best made by cystoscopy and by stereoscopic cystography. The absence of any pathognomonic subjective symptoms, except the notable symptom of prolonged urinary dysfunction in childhood and adolescence, make the clinical history of less value than usual.

*Differential Diagnosis*—In the diagnosis of this rare type of anomaly it must be differentiated from all other processes obstructive to urination. One must consider prostatic hypertrophy, hypertrophy of the interureteral ridge, neurogenic changes in the bladder, diverticulum and, from the cystographic aspect, urachal cysts and diverticula.

*Treatment*—The treatment should be directed toward relief of any obstruction at the neck of the bladder, and from our experience in this one case, we believe that resection of the diaphragm or ledge is indicated. Our patient at the time of writing has no residual urine.

#### SUMMARY AND CONCLUSIONS

A case of true hour-glass bladder is reported, probably the sixth or seventh of this type (Blum's type II) in the literature.

Considerations of its etiology are discussed, and they coincided entirely with the views of Pagenstecher and Gruber.

While it is impossible to contradict categorically the theoretical considerations advanced by Krasa and Paschkis and by Chwalla, we are inclined to the opinion that their hypotheses are too sharply defined in the light of the present incomplete understanding of the pathogenesis of this anomaly.

Surgical treatment is to be directed toward any obstruction at the neck of the bladder, and resection of the constricting band appears to be indicated.

A remarkable return toward normal function and normal outline of the bladder is evidenced by cystograms made a year after resection of the neck.

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may be one reason that more ulcers did not develop. This method of feeding hydrochloric acid failed to produce any chronic ulcers, as proved by microscopic study of the ulcers. In 6 dogs there was associated mild to marked gastritis and duodenitis, whereas in 2 of the 8 animals no lesions demonstrable either grossly or microscopically were evident, even after experimental periods of thirteen and twenty-five days, respectively. In any study of gastric analysis in dogs it must be remembered that values for acidity are extremely variable, in that normal values for acidity may be obtained one day and subnormal values or even hyperacidic values the next day (table 1). It has been shown repeatedly and statistically by

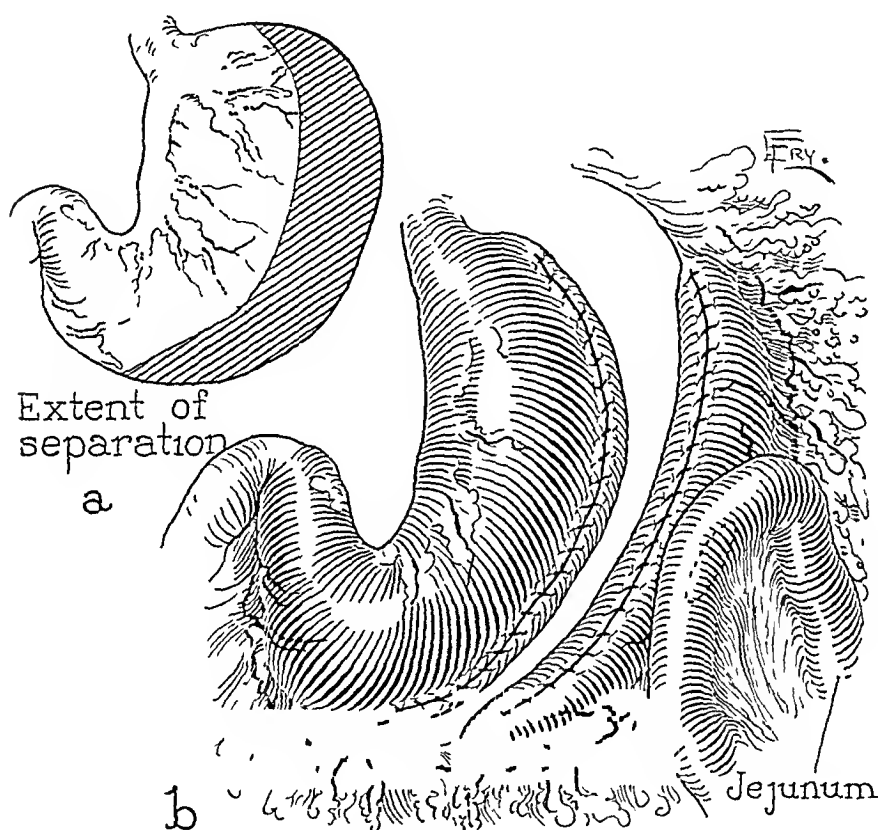


Fig 1—The drawing in the upper left hand corner (*a*) shows the extent of resection of the region of the greater curvature or the amount of the stomach to be incorporated into a gastric pouch. The larger drawing (*b*) illustrates the formation of a pouch from the greater curvature, with a side-to-side anastomosis of a loop of the proximal jejunum to this pouch.

Laspeyres<sup>57</sup> and others that even in human beings this variability from anacidity to hyperacidity obtains in persons both in health and in disease, though to a less extent than in animals. This variability has been demonstrated in our own experiments in the gastric analyses on the controls. However, a study of the acidity values for the entire period of experimentation with repeated feeding

<sup>57</sup> Laspeyres, R. Centralbl f d Grenzgeb d Med u Chir 5 25, 157 and 225, 1902.

# RELATIONSHIP OF GASTRIC ACIDITY TO PEPTIC ULCERATION

I EFFECT OF HYDROCHLORIC ACID, OF HISTAMINE AND OF  
DEVIATION OF BILE

MIMS GAGE M D

ALTON OCHSNER, M D

AND

KIYOSHI HOSOI, M D

NEW ORLEANS

The relationship of gastric acidity to peptic ulceration has been debated for years. Volumes have been written, supported by clinical, statistical and experimental data, on the subject of the primary etiologic factors in the genesis of peptic ulceration. From the present knowledge, it is safe to assume that no one factor can be held responsible for ulcer in general. Several factors are usually operative in the causation and prolongation of the ulcerous condition, or, according to Tendeloo,<sup>1</sup> there is a constellation of factors. Indeed, Alvarez<sup>2</sup> reminded his readers that there may be several types of the disease in different parts of the world. It is this very complexity of causes that has been the incentive of much experimentation. The present tendency is to consider peptic ulceration as a local manifestation of systemic disease or of disease elsewhere in the body rather than as an involvement sui generis of the stomach or duodenum. The nature of the local manifestation however, has given rise to much discussion. It cannot be denied that purely local causes, such as direct violence and corrosive poisons, may produce acute ulcers. Excellent reviews on the pathogenesis of peptic ulcer have been made by Hurst,<sup>3</sup> Halperin,<sup>4</sup> Smithies,<sup>5</sup> Held and Goldbloom,<sup>6</sup> Raine<sup>7</sup> and Carnot and Gaehtlinger.<sup>8</sup> Clinically, we have come to the conclusion that whereas there are many important factors responsible for the causation and persistence of peptic ulcer, the three most important are (1) the inherent predisposition to formation of ulcer,

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1 Tendeloo, N P. *Berl Klin Wchnschr* 58 1 1921

2 Alvarez W C. *Am J Surg* 18 207 1932

3 Hurst, A F. *Guy's Hosp Rep* 74 413 1924

4 Halperin, G. *Internat Abstr Surg* 43 173 1926

5 Smithies, T. *Ann Clin Med* 4 468 1925

6 Held, I W and Goldbloom, A A. *M Clin North America* 1 319, 1930

7 Raine, F. *Wisconsin M J* 30 540 1931

8 Carnot, P and Gaehtlinger, H. *Paris med* 1 309 1931

of hydrochloric acid showed that in general there was a tendency toward achlorhydria, chlorides continued to be secreted, but at a low level (table 1). No acceptable explanation has as yet been given as to why under certain conditions the stomach loses its ability to secrete free hydrochloric acid but is still able to secrete chlorides. But there was a return to normal values for free hydrochloric acid after a month or so of experimentation, even though the administration of hydrochloric acid was not stopped. Thus, it is seen that the parietal cells of the stomach recover from the toxic or corrosive effect of the repeated feedings. The highly corrosive concentration of acid used experimentally by others and by us can never obtain in the human stomach, even in disease, because the intrinsic or extrinsic mechanisms of neutralization rapidly reduce any high acidity to 0.15 per cent hydrochloric acid.

Injections of histamine in 7 animals caused varying degrees of anemia of the tissues. In contrast to the pink appearance of tissues of presumably healthy dogs, the various viscera appeared very pale in the dogs treated with histamine. From a mild to marked gastritis and duodenitis were present in all 7 (100 per cent) animals, and in 1 these conditions were the only demonstrable disturbance, even after five months' experimentation with histamine. The gastritis appeared to be limited to the pyloric antrum and involved the entire stomach only when it was present to a marked degree. There were also hemorrhages (4 dogs), erosions (1 dog) and acute ulcers (3 dogs, or 43 per cent), which were usually multiple. In one animal (HH 43), which had received injections over a period of one hundred and thirty-four days, there were twenty-two ulcers of various sizes and depths (fig. 6). These ulcers were most frequently or most abundantly found along the lesser curvature, confirming the usual clinical observation that peptic ulcers occur along the lesser curvature of the pylorus. Histamine was found to produce ulcers but did not stop them from healing, as evidenced by the microscopic picture of encroachment of marginal epithelium over the floor of the ulcer. Also, there was microscopic evidence of increased production of mucus, shown by the prominence everywhere of the distended mucous cells of the gastric mucosa. Histamine does not appear to cause hyperacidity or hypo-acidity of exhaustion, even after from four to five months of injections (table 2). The values for acidity obtained were usually within the range of normal variations for dogs (table 2), although the values after stimulation with histamine in dogs with a pouch with anastomosis from the pouch to the jejunum were frequently double the pre-operative values without histamine stimulation. Gastric analyses in at least 2 animals (HH 50 and 83) showed this definitely.

EXPERIMENT 2—*Observations on dogs with extirpated (a) greater curvature (fig. 1a) and (b) lesser curvature (fig. 2)*

The greater curvature of the stomach was extirpated in 30 animals, only 11 of which lived sufficiently long for satisfactory observations to be made. The lesser curvature was extirpated in 6 animals, 4 of which survived long enough for sufficient observations. Practically all the respective curvatures were extirpated, the actual amount removed depending almost entirely on the size of the stomach. Black silk sutures were used throughout, but later all hemostatic sutures were made with no. 0 chromic catgut, the silk being employed only for the seromuscular layer. Extirpation of the greater or lesser curvatures of the stomach in dogs did not significantly change the values for acidity of the gastric contents of the main portion of the stomach when compared with the preoperative values (tables 3 and 4). In the control groups of animals receiving no hydrochloric acid or hista-

i e, ulcer diathesis, (2) susceptibility of the tissue and (3) increased gastric acidity. If this conception of the problem is correct, the clinician's therapeutic endeavors should be directed toward controlling the gastric secretion and acidity, because there is probably little that can be done to change the inherent predisposition and susceptibility of the tissue.

The acidity of freshly secreted pure gastric juice is at about the level of 0.5 per cent hydrochloric acid, which is rapidly reduced to that of 0.15 per cent hydrochloric acid during digestion. This self-regulation of the acidity of the contents of the stomach is effected through the following factors (Bennett,<sup>9</sup> Babkin<sup>10</sup>) (1) saliva and food materials, (2) gastric mucus, (3) regurgitated duodenal contents, (4) variations in the acidity of the gastric juice and (5) the water and chloride content of the body. Abundant clinical and experimental evidence is now at hand to show that there is a reflux of bile and pancreatic juices into the stomach (Moppert,<sup>11</sup> Apperly,<sup>12</sup> Medes and Wright<sup>13</sup>) Iwanow<sup>14</sup> and Wright and Medes<sup>15</sup> noted at times a marked dissociation of the regurgitation of bile and of pancreatic juice.

Numerous experiments have been devised to study the protective influence of the alkaline duodenal contents in the prevention of peptic ulceration. The underlying principle of all the different methods is the same, whether duodenal contents are deviated in toto or separately as bile, pancreatic juice or succus entericus. The experiments of Patrie,<sup>16</sup> Mann<sup>17</sup> and others have shown how technically simple it is to anastomose the pancreatic or bile ducts into other hollow viscera. Mann and Williamson<sup>18</sup> in this country and Weiss and his associates<sup>19</sup> in France have done much to popularize the method of "duodenal drainage." The entire duodenal contents have been deviated by the various methods of duodenectomy, with loss of both the bile and the pancreatic juice,

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TABLE 3—*Preoperative and Postoperative Values for Hydrochloric Acid After a Test Meal in Animals Following Resection of the Greater Curvature of the Stomach*

Dog	Preoperative Controls				Postoperative Controls				Duration, Days	Ulcer
	Date	Hydrochloric Acid			Date	Hydrochloric Acid				
		Free	Combined	Total		Free	Combined	Total		
HH 16	1/21/32	35	28	63	2/25/32	11	9	20*	33	Ulcers
	1/22/32	27	12	39	3/ 4/32	18	16	34		
	1/28/32	14	9	23*	3/10/32	0	9	9		
	1/29/32	45	11	56*	3/17/32	0	4	4		
	2/ 4/32	40	19	59	3/24/32	25	12	37		
	2/ 5/32	20	10	30						
HH 18	1/22/32	50	17	67	2/25/32	15	18	33	16	None, anemia
	1/28/32	55	10	65	3/ 4/32	25	7	32		
	1/29/32	42	5	47*	3/10/32	27	12	39		
	2/ 4/32	55	10	65*						
	2/ 5/32	42	11	53*						
HH 34	3/10/32	21	23	44	4/ 7/32	49	19	68	103	None
	3/17/32	33	25	58	4/15/32	39	15	54		
	3/21/32	36	11	47	4/21/32	29	21	50		
					4/29/32	40	24	64		
					5/ 5/32	0	42	42		
					5/11/32	70	17	87		
					5/19/32	63	18	81		
					5/27/32	35	18	53		
					6/ 2/32	57	20	77		
					6/10/32	32	12	44		
					6/18/32	55	18	73		
					6/24/32	55	18	73		
					6/30/32	53	17	70		
					7/ 8/32	28	24	52		
					7/14/32	20	5	25		
HH 37	3/17/32	35	25	60	4/ 7/32	55	25	80	47	Ulcers of pylorus
	3/21/32	36	30	66	4/ 9/32	33	22	56		
					4/21/32	32	32	64		
					4/29/32	21	29	50		
					5/ 5/32	37	30	67		
					5/11/32	44	37	81		
					5/19/32	38	12	50		

\* Bile

TABLE 4—*Preoperative and Postoperative Values for Hydrochloric Acid After a Test Meal in Animals Following Resection of the Lesser Curvature of the Stomach*

Dog	Preoperative Controls				Postoperative Controls				Duration, Days	Ulcer
	Date	Hydrochloric Acid			Date	Hydrochloric Acid				
		Free	Combined	Total		Free	Combined	Total		
HH 74	8/15/33	20	19	39	9/ 7/33	0	14	14*	84	None
	8/17/33	14	17	31	10/ 5/33	30	10	40		
					10/13/33	0	10	10*		
					10/19/33	0	10	10*		
					10/27/33	40	25	65		
					11/ 2/33	39	12	51		
					11/10/33	18	10	28		
HH 107	11/ 9/33	8	8	16	12/ 1/33	0	5	5*	65	None
	11/10/33	14	4	18	12/ 8/33	5	5	10		
					12/14/33	49	11	60		
					12/22/33	0	17	17*		
					12/28/33	16	24	40		
					1/ 5/34	0	5	5*		
					1/11/34	8	10	18*		
					1/19/34	7	16	23		
HH 108	11/ 9/33	22	14	36	12/ 1/33	0	5	5*	13	None
	11/10/33	0	10	10*						

\* Mucus

to the outside, or by the method of duodenal drainage, with conservation of these juices, into the lower portion of the small intestine (Steinberg,<sup>20</sup> Mann<sup>21</sup>), appendix (Winkelbauer and Hogenauer<sup>22</sup>), cecum, rectum (Leriche<sup>23</sup>), pelvis of the kidney (Kapsinow<sup>24</sup>) or urinary bladder (Leriche and his associates<sup>25</sup>). In these operations for the establishment of duodenal drainage the line of deviation is made in the proximal portion of the duodenum itself (Langenskiöld<sup>26</sup>), at the pyloric sphincter (Mann and Williamson) or in the pylorus (Morton,<sup>27</sup> McCann,<sup>28</sup> Exalto,<sup>29</sup> Winkelbauer and Hogenauer). Of course, in all, the continuity of the gastro-intestinal tract is reestablished. A survey of the enormous literature on operations for the establishment of duodenal drainage and of the results obtained by these careful investigators shows that there is indeed a great variation from Ivy's<sup>30</sup> 5 per cent to Morton's<sup>27</sup> 100 per cent incidence of jejunal ulcer following duodenal drainage. Mann<sup>21</sup> and Owings and Smith,<sup>31</sup> after obtaining typical chronic jejunal ulcers by duodenal drainage, secured healing of these ulcers by reconducting the duodenal contents over the ulcerated areas. Even an ulcer which had perforated the entire thickness of the jejunal wall would almost entirely disappear within twenty-five days after it was protected from the gastric contents. When the alkaline digestive juices were again short-circuited, the ulcer reformed. Mann maintained that although the great importance of chemical factors is recognized, the mechanical factors involved in the production of ulcer are not suffi-

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mine ulcers did not develop in the 3 in which the lesser curvature was resected and did develop in 2 (50 per cent) of the 4 in which the greater curvature was resected

Feeding of hydrochloric acid to dogs with extirpation of the greater curvature produced multiple erosions of the pylorus in 2 of 3 dogs (HH 24 and 46) In the third dog (HH 44), with no erosions, moderate gastritis of the pyloric mucosa was found This is interesting, because this particular dog received 1 per cent hydrochloric acid by stomach tube three times daily every other day for forty-seven days A study of the gastric analyses performed one hour after the feeding of hydrochloric acid shows that the dog's stomach was able to neutralize rapidly this concentration of acid to within normal limits (table 5) Regurgitation of bile is probably not a factor in this neutralization, since no bile was found in the

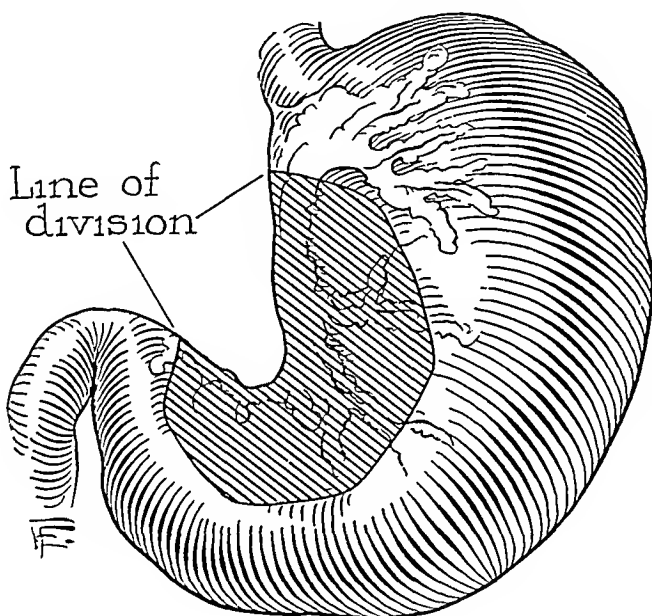


Fig 2—A drawing showing the extent of extirpation of the region of the lesser curvature or the amount of the region of the lesser curvature to be incorporated into a gastric pouch

21 samples of the gastric contents in this control group (3 animals) receiving hydrochloric acid and since the combined values for hydrochloric acid were always lower than those for free hydrochloric acid in 2 (HH 24 and 44) of the 3 animals After stimulation with histamine the values for acidity remained within normal limits (table 6), and acute ulcers were produced in 2 (HH 40 and 15) of 4 dogs with extirpation of the greater curvature, 1 of which also showed acute erosions (HH 40) After repeated stimulation with histamine no erosions or ulcers were found (table 7) in 1 animal (HH 101) with extirpation of the lesser curvature Stimulation with histamine evidently did not increase the incidence of gastric erosions or ulcerations in this group The absence of erosions or ulcerations in the group with extirpation of the lesser curvature and their formation in the group with extirpation of the greater curvature appear to support the theory

ciently appreciated. A jejunal ulcer develops at the site of greatest impingement by the acid gastric contents—lateral and posterior to the central axis of the intestine. Mann and Bollman<sup>32</sup> concluded that in the prevention of peptic ulcer duodenal mucosa and secretion are probably the most important factors, bile is of least importance and pancreatic secretion is intermediate between the two. On the other hand, Graves<sup>33</sup> and DeBakey,<sup>34</sup> working in the experimental laboratory at Tulane University, observed that bile was probably the most important alkaline secretion in the prevention of peptic ulceration, that duodenal secretions (succus entericus) were least important and that pancreatic juice occupied an intermediate position. From the experiments recorded in the literature on total or isolated deviation of the alkaline duodenal contents, the following conclusions are indicated. The sensitivity of the intestinal mucosa to ulceration increases progressively from the duodenum to the ileum. Total deviation of the alkaline duodenal contents is more effective in producing ulceration than the isolated deviation of duodenal, biliary or pancreatic secretions. The question of experimental reflux of the entire duodenal contents into the stomach in the prevention of peptic ulceration is a subject still sub judice, although there is much evidence to show that this can prevent peptic ulceration or, if an ulcer is already present, promote its healing.

Artificial hyperacidity produced experimentally by the feeding of hydrochloric acid (Bolton,<sup>35</sup> Langenskiöld, Mann and Bollman, Friedenwald, Feldman and Morrison<sup>36</sup>) results in the formation of erosions and ulcerations, but it does not prevent their healing, except when highly corrosive concentrations are used. Obviously such high concentrations are not found in the human stomach, even in one which is the seat of peptic ulceration. Instead of feeding hydrochloric acid one can stimulate gastric secretion in laboratory animals and in man by the subcutaneous, intramuscular or intravenous injection of histamine (Popielski,<sup>37</sup> Best and McHenry<sup>38</sup>). Hence it is natural that histamine should be used to produce peptic ulcer experimentally by its stimulating effect on the

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32 Mann, F. C., and Bollman, J. L. Experimentally Produced Peptic Ulcers, *J. A. M. A.* **99** 1576 (Nov. 5) 1932.

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TABLE 5—*Incidence of Ulcers in Animals with the Greater Curvature of Stomach Removed Following Feeding with Hydrochloric Acid*

Dog	Acidity Before Administration of 1% Hydrochloric Acid				Acidity After Administration of 1% Hydrochloric Acid				Dura- tion, Days	Ulcer
	Date	Hydrochloric Acid			Date	Hydrochloric Acid				
		Free	Com- bined	Total		Free	Com- bined	Total		
HH 24	2/12/32	29	21	50	2/24/32	15	17	32	67	Erosions, gastritis duodenitis
	2/15/32	48	16	64	4/ 1/32	50	11	61		
	2/18/32	10	16	26	4/ 7/32	49	9	58		
	2/19/32	25	22	47	4/15/32	27	14	41		
	2/25/32	40	11	51	4/21/32	31	12	43		
					4/29/32	35	15	50		
					5/ 5/32	18	15	33		
					5/11/32	41	13	54		
				5/19/32	35	10	45			
HH 44	4/ 1/32	38	16	54	4/21/32	40	19	59	47	Gastritis
	4/ 4/32	63	21	84	4/29/32	15	10	25		
					5/ 5/32	22	19	41		
					5/11/32	11	12	23		
					5/19/32	27	13	40		
					5/27/32	14	9	23		
					6/ 2/32	20	10	30		
HH 46	4/ 7/32	56	28	84	5/ 5/32	0	21	21	37	Erosions gastritis
	4/12/32	29	21	50	5/11/32	0	11	11		
					5/19/32	9	16	25		
					5/27/32	16	14	30		
					6/ 2/32	6	16	22		

TABLE 6—*Incidence of Ulcers in Animals with the Greater Curvature of the Stomach Removed Following the Subcutaneous Injection of Histamine*

Dog	Acidity Before Injections of Histamine				Acidity After Injections of Histamine				Dura tion Days	Ulcer
	Date	Hydrochloric Acid			Date	Hydrochloric Acid				
		Free	Com bined	Total		Free	Com bined	Total		
HH 39	3/17/32	13	12	25	4/15/32	0	13	13*	120	Gastritis
	3/21/32	9	12	21	4/21/32	57	18	75		
					4/29/32	62	20	82		
					5/ 5/32	39	22	61		
					5/11/32	28	22	50		
					5/19/32	30	13	43		
					5/27/32	28	12	40		
					6/ 2/32	33	9	42		
					6/10/32	28	10	38		
					6/16/32	65	13	78		
					6/24/32	38	10	48		
					6/30/32	30	14	44		
					7/ 8/32	15	10	25		
					7/14/32	29	20	49		
					7/22/32	32	22	54		
					7/28/32	22	14	36		
					8/ 5/32	39	23	62		
HH 40	3/17/32	20	12	32	4/15/32	0	31	31	13	Ulcers erosions
	3/21/32	20	11	31	4/21/32	6	24	30		
HH 45	4/ 1/32	14	51	65	4/21/32	5	11	16	16	Gastritis
	4/ 4/32	18	19	37	4/29/32	0	26	26		
HH 15	1/ 5/32	0	29	29	2/15/32	41	20	61	27	Ulcers
	1/ 7/32	39	16	55	2/19/32	15	20	35		
	1/11/32	18	18	36	2/25/32	54	32	86		
	1/12/32	4	22	26	3/ 4/32	57	18	75		

\* Bile

has tried to save his patient from an operation and, in so doing, the patient's life has been jeopardized. So the patient goes to the hospital and either has a long stormy course, which may be of great economic loss, or else dies. The result is that the hospital and the surgeon are blamed, and the practitioner is completely exonerated. From the standpoint of economy alone the public should learn that the conservative and economic treatment of acute appendicitis is early prompt operation.

7 In times like the present one, the practitioner may choose to operate on the patient himself, or the family may request it. He is the "occasional operator." He frequently lacks operating privileges in some of the larger, better equipped hospitals. So the patient may be taken to a smaller private hospital. At operation, the physician may encounter a situation with which he is entirely unable to cope. Appendectomy may be the simplest or the most difficult operative procedure. He lacks the judgment and skill and experience in making important decisions and in executing technical maneuvers. Dire events then take place. One complication follows another. The hospital may be inadequately equipped to meet the demands for certain important treatments and emergencies. A death results which might have been prevented in proper hands. The public must be taught the importance of receiving skilled care in a well equipped hospital.

8 Instruction to high school and university students as recommended by the Philadelphia group, is an excellent plan, because it is known that the highest incidence of appendicitis occurs between the ages of 13 and 30. Such a policy could be introduced into large business concerns and corporations. The program to reduce the mortality from appendicitis in Philadelphia is being conducted so successfully that there has been a real diminution in fatalities, and consequently in the death rate, in the past five years.

These are not original or new ideas. They have been repeatedly emphasized in the literature. It is the real duty of the public health service, of the county, state and national medical societies and of the insurance companies to present these facts in an intelligent dispassionate manner before the public. It would be extremely unwise to employ alarmist tactics because many persons with vague pains on the right side would soon find their way to the operating table to undergo an utterly useless and unnecessary appendectomy. One is confronted, therefore, with the present danger of insufficient public education on the one hand and the treachery of overenthusiastic propaganda on the other. Concerted, well directed, organized action could be made to follow the middle course.

#### SUMMARY

The total mortality rate from acute appendicitis at the Presbyterian Hospital from 1916 to 1933, inclusive, is 5.08 per cent, or 135 deaths

in 2,653 cases. The total death rate for each of the five groups is as follows: acute appendicitis, 0.59 per cent; acute appendicitis with acute local peritonitis, 1.9 per cent; acute appendicitis with peritoneal abscess, 10.5 per cent; acute appendicitis with acute diffuse (diffusing, spreading) peritonitis, 17.02 per cent; and acute appendicitis with progressive fibrinopurulent peritonitis, 88 per cent.

The curve of the progressive five year average of total deaths from acute appendicitis in all groups (from 1 to 5) shows a moderate, general decrease (chart 10). The five year average mortality curves of groups 1 and 2 indicate a decrease, but groups 3 and 4 disclose a definite, alarming increase, compared to earlier five year periods (chart 11).

An analysis of the deaths and a discussion of certain means of preoperative, operative and postoperative preventive measures have been presented for each of the groups (except group 4, which will be reported on in detail in another paper).

There is need for proper public education in the attempt to effect a general reduction in the mortality rate of acute appendicitis. The surgeon and the practitioner must also learn to recognize the atypical case early.

The death rate from acute appendicitis and its associated lesions can, and must, be reduced.

that the resection of the regions of the lesser curvature at the angle of reentrance prevents the formation of peptic ulcer

EXPERIMENT 3—*Observations on dogs with a Heidenham (fig 1b) or Pavlov pouch (fig 3)*

A pouch of the greater curvature (Heidenham) with jejunal anastomosis was made in 6 animals, all of which survived sufficiently long for the observations

TABLE 7—*Incidence of Ulcers in Animals with the Lesser Curvature of the Stomach Removed Following the Subcutaneous Administration of Histamine*

Dog	Date	Acidity Before Injections of Histamine			Acidity After Injections of Histamine			Dura- tion, Days	Ulcer		
		H <sub>3</sub> drochloric Acid			Hydrochloric Acid						
		Free	Com- bined	Total	Free	Com- bined	Total				
HH 101	10/13/33	25	20	45	11/16/33	20	12	32	62	None	
	10/17/33	30	15	45	11/24/33	10	10	20*			
					12/ 1/33	0	10	10			
Po-operative values					12/ 8/33	13	8	21			
11/15/33					8	14	22	12/13/33	15	20	35
								1/ 5/34	31	9	40
								1/11/34	31	22	53

\* Mucus

TABLE 8—*Incidence of Ulcers in Animals with Heidenham Pouch of the Greater Curvature of the Stomach Anastomosed to the Jejunum Following the Administration by Mouth of Dilute Hydrochloric Acid*

Dog	Date	Acidity Before Injections of Histamine			Date	Acidity After Injections of Histamine			Duration Days	Ulcer
		Hydrochloric Acid				Hydrochloric Acid				
		Free	Combined	Total		Free	Combined	Total		
HH 49	5/27/32	29	18	47	6/24/32	0	11	11	11	Erosions and ulcers of jejunum
	6/ 2/32	37	17	54	6/ 9/32	0	15	15*		
HH 50	6/23/32	6	6	12	7/22/32	17	23	40	64	Ulcers of pylorus gastritis perforated jejunal ulcer
	6/24/32	14	6	20	7/28/32	5	10	15		
Post-operative values-					Entirely mucus					
	7/ 8/32	1	12	25	8/11/32	7	41	48		
	7/14/32	0	29	29	8/19/32	25	21	46		
					8/25/32	26	17	43		
					9/ 2/32	20	47	67		
					9/ 8/32	25	24	49		
					9/16/32	45	10	55		
HH 51	5/19/32	21	27	58	6/24/32	42	22	64	64	Gastritis erosion of duodenum marginal and jejunal ulcers
	5/27/32	13	11	24	6/ 9/32	41	10	51		
					7/ 8/32	19	19	38		
					7/14/32	40	21	61		
					7/22/32	5	28	33		
					7/28/32	4	22	26		
					8/ 5/32	22	17	39		
					8/11/32	21	21	42		
					8/19/32	42	16	58		
					8/25/32	15	10	25		

\* Mucus

to be completed. A pouch of the lesser curvature (Pavlov) with jejunal anastomosis was made in 27 animals only 7 of which lived sufficiently long for observations to be made. In our experiments with the pouch of the greater curvature (modified Heidenham type) with jejunal anastomosis (simulating Meckel's diver-





Fig 8 (dog HH 83) —Histamine was injected three times daily on alternate days over a period of twenty-seven days. The probe passed through the stoma of the gastrojejunal anastomosis into the gastric pouch. There are three jejunal ulcers (1, 2 and 3). Ulcer 3 had perforated into the general peritoneal cavity. Careful microscopic studies reveal that none of these ulcers are marginal, all being located strictly in the jejunum proper.

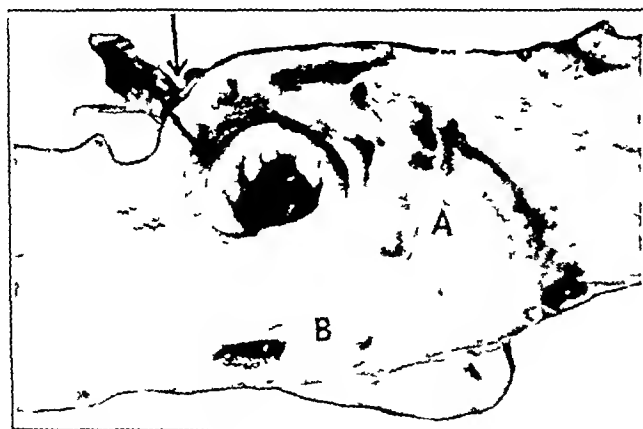


Fig 9 (dog HH 88) —Control animal observed for one hundred and fifty-two days. Two chronic jejunal ulcers are present (A and B). The base of each is filled with granulation tissue and shows evidence of healing along the edges. The arrow points to a loose silk thread hanging into the lumen, which has not caused any ulceration.

ticulum containing gastric mucosa), acute, subacute or chronic jejunal ulcers were produced in each of 6 animals (100 per cent). The ulcers were in the efferent loop in 5 dogs and both in the efferent loop and at the anastomotic stoma in 1 dog (HH 51). These ulcers had a tendency to perforate, since 5 of the 6 animals died of peritonitis following perforation (fig 7). Stimulation with histamine did not increase this tendency to perforation of an anastomotic ulcer, as 2 of 3 dogs receiving histamine had perforated jejunal ulcers whereas all 3 control animals, which did not receive histamine, had perforated ulcers. In 1 (HH 47) of these control animals, there were two chronic gastric ulcers (located in the main portion of the stomach) in addition to the perforated jejunal ulcer. Gastric analyses showed values for acidity to be within normal variations (tables 8 and 9). Stimulation with histamine did not prevent an anastomotic ulcer from undergoing

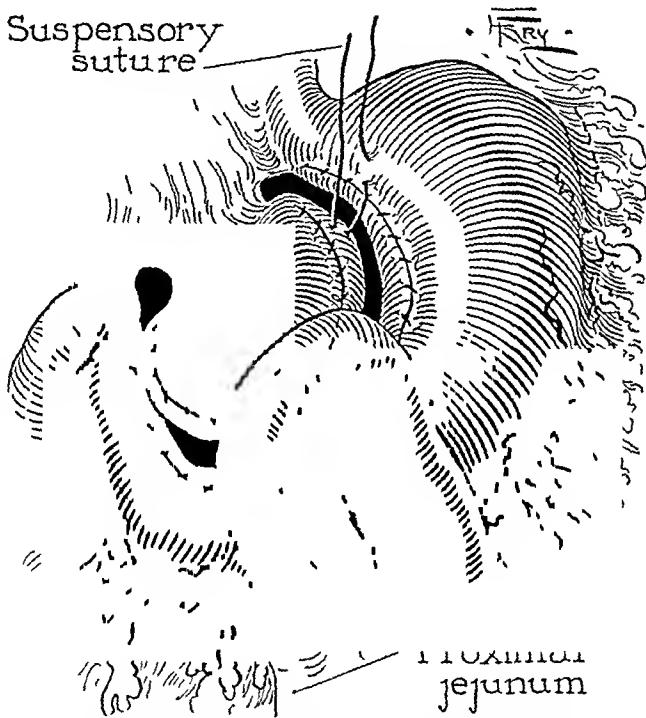


Fig 3—A drawing showing the formation of a gastric pouch from the lesser curvature and anastomosis of a loop of the proximal jejunum. Note the suspensory suture to prevent the pouch from being pulled or stretched subsequently.

a healing process, as shown by the microscopic study of one of these jejunal ulcers. The animal (HH 49) in which there was this tendency of the ulcer to heal had been receiving 0.8 mg of histamine per kilogram of body weight three times daily on alternate days during a period of eleven days. Because of the predilection of jejunal ulcers for the efferent loop, a careful study of the jejunal loop anastomosed to the gastric pouch was made. It was noted that the proximal or afferent loop was always normal in appearance, whereas the distal or efferent loop showed the effects of the irritating acid secretions from the gastric pouch passing through it. The efferent loop was edematous and congested, with numerous various-sized petechiae and hemorrhages and even erosions. Microscopic studies revealed subacute or chronic jejunitis, depending on the duration of the experiment.

illustrated in experiment 2, in which extirpations of the lesser and the greater curvature were performed. As mentioned earlier, the incidence of ulceration was considerably higher (63.6 per cent) in the animals with the greater curvature removed than it was (0 per cent) in those in which the lesser curvature was removed. The acid secretion is primarily from the greater curvature and fundus of the stomach, which is generally accepted, and it would seem probable that if acidity were the only factor the incidence of ulceration should be higher in the animals with the greater curvature present. As the reverse was present, however, it is evident that susceptibility of the tissue is an important factor in the causation of peptic ulcer.

Much has been written, based on clinical and experimental data, in favor of the view that the use of nonabsorbable suture material in gastro-intestinal anastomosis may be of etiologic importance in the causation of ulceration. It is customary not to use silk thread or other nonabsorbable suture material for the hemostatic suture on the mucosa. In spite of the fact that black silk was used only for the seromuscular suture and no 00 chromic catgut was used for the hemostatic suture in all our experiments, at necropsy loose silk threads were found hanging in the lumen of the main portion of the stomach, or in the stoma of the gastrojejunostomy or of the cholecystogastrostomy (6 animals). The silk thread must have produced at least some irritation of the mucosa in a mechanical way at its point of emergence, but in no instance was an ulceration produced by the thread in our animals (figs 9 and 10). In 1 dog the silk thread used for the Lembert suture was found at necropsy hanging loose in the stoma of the cholecystogastrostomy and heavily encrusted with bile salts. Yet there was no ulceration. Although silk threads have been found associated with ulcers of the stomach in some of the cases reported in the literature, it is questionable whether they play an important rôle in the production of peptic ulceration in man.

*Jejunal Ulceration*—The importance of mucosal susceptibility and hyperacidity in the production of peptic ulcer was illustrated by the results obtained in experiments 3 and 4. In experiment 3 a gastric pouch was formed from either the greater or the lesser curvature and anastomosed to the jejunum. Of 6 dogs in which a pouch of the greater curvature was formed and anastomosed to the jejunum, ulcers developed in all (100 per cent) whether the animal received injections of histamine (3 dogs) or not (3 dogs). In this experiment the condition simulated Meckel's diverticulum containing gastric mucosa, in which the incidence of peptic ulcer of the diverticular mucosa is high. Of 7 animals in which a pouch of the lesser curvature was made and anastomosed to the jejunum, ulcers developed in 5 (71 per cent). The explanation for the ulceration in these animals is that the jejunal mucosa, not being

TABLE 9—Incidence of Ulcers in Control Animals with Heidenham Pouch of the Greater Curvature of the Stomach Anastomosed to the Jejunum

Dog	Preoperative Controls				Postoperative Controls				Duration, Days	Ulcer
	Date	Hydrochloric Acid			Date	Hydrochloric Acid				
		Free	Com bined	Total		Free	Com bined	Total		
HH 47	5/19/32	28	8	36	6/24/32	10	16	26	78	Ulcers of pylorus perforated jejunal ulcer
	5/27/32	9	13	22	6/30/32	18	29	47		
	6/ 9/32	11	31	42	7/ 8/32	20	15	35		
	6/10/32	28	15	43	7/14/32	5	25	30		
					7/22/32	5	24	29		
					7/26/32	23	22	45		
					8/ 5/32	40	18	58		
					8/11/32	20	22	42		
					8/19/32	48	19	67		
					8/25/32	33	19	52		
HH 48	5/19/32	5	10	15	9/ 2/32	15	17	32	71	Perforated jejunal ulcer
	5/27/32	18	28	46	6/24/32	18	20	38		
					6/30/32	23	20	43		
					7/ 8/32	5	25	30		
					7/22/32	37	17	54		
					7/26/32	24	15	39		
					8/ 5/32	19	7	26		
					8/11/32	32	21	53		
					8/19/32	20	14	34		
					8/25/32	27	13	40		
HH 52	5/19/32	33	5	38	Died 6/23/32 just after rest period, 16 days postoperatively				Perforated jejunal ulcer	
	5/27/32	22	10	32						

TABLE 10—Incidence of Ulcers in Animals with Modified Pavlov Pouch of the Lesser Curvature of the Stomach Anastomosed to the Jejunum Following the Administration of Histamine Subcutaneously

Dog	Acidity Before Injections of Histamine				Acidity After Injections of Histamine				Dura- tion, Days	Uleer	
	Date	Hydrochloric Acid			Date	Hydrochloric Acid					
		Free	Com- bined	Total		Free	Com- bined	Total			
HH 83	9/ 8/33	10	10	20	10/ 5/33	75	20	95	27	Uleers of jejunum perforated jejunal ulcer	
	9/12/33	5	10	15	10/13/33	12	18	30			
					10/19/33	0	42	42			
HH 93	9/15/33	37	18	55	10/ 9/33	20	15	35	24	Perforated jejunal ulcer	
	9/19/33	46	14	60	10/13/33	0	20	20*			
					10/19/32	0	10	10*			
					10/27/33	0	10	10*			
HH 89	9/15/33	18	7	25	10/13/33	7	23	30	157	Uleer of jejunum	
	9/19/33	44	22	66	10/19/33	21	11	32			
					10/24/33	13	47	60			
Postoperative values					11/ 2/33	28	18	46			
10/ 5/33					30	15	45	11/10/33	10	14	24
								11/16/33	0	58	58
								11/24/33	35	12	47
								12/ 1/33	15	28	43
								12/ 8/33	41	17	58
								12/14/33	45	25	70
								12/22/33	22	18	40
								12/28/33	16	8	24
								1/ 5/34	29	30	59
								1/11/34	64	24	88
								1/19/34	71	21	92
								1/25/34	60	20	80
								2/ 2/34	52	34	86
								2/ 8/34	41	23	64
								2/16/34	23	9	32
								2/22/34	49	9	58
								3/ 2/34	37	8	45

\* Mucus

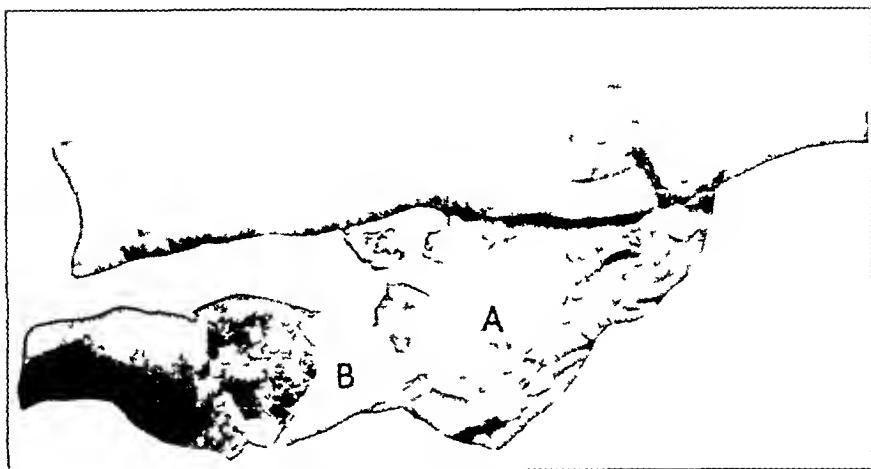


Fig 10 (dog HH 76)—Histamine was injected three times daily on alternate days over a period of one hundred and twenty-seven days. A chronic callous jejunal ulcer had formed opposite the anastomosis between the gastric pouch and jejunal loop. Note that there is no relationship between this ulcer and the silk thread hanging into the lumen. *A* indicates the gastric pouch and *B*, the gall-bladder to which a piece of liver is attached.

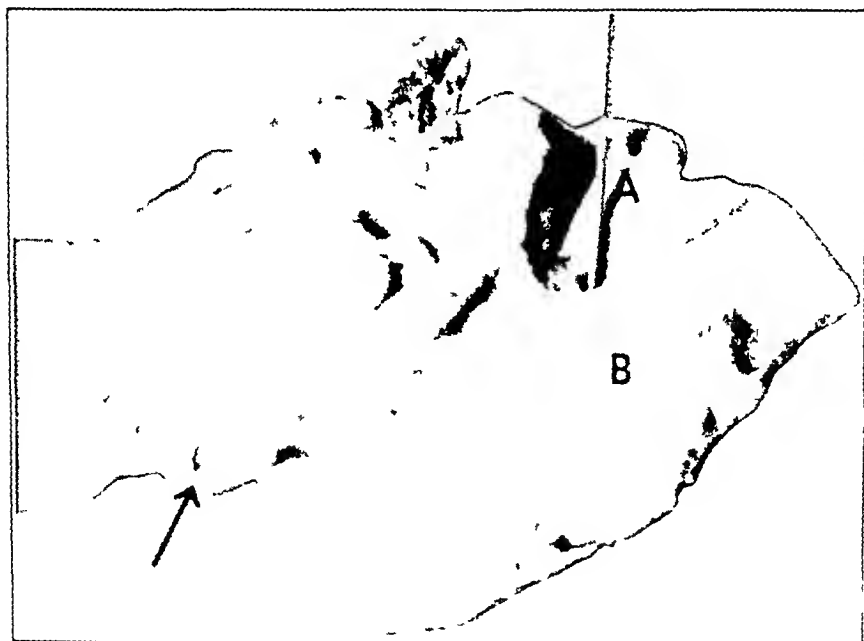


Fig 11 (dog HH 113)—A control animal observed for ten days postoperatively. The probe is inserted into a perforated marginal ulcer between the gastric pouch *A* and the jejunum *B*. The arrow points to a chronic duodenal ulcer.

TABLE 11—*Incidence of Ulcers in Control Animals with Modified Pavlov Pouch of the Lesser Curvature of the Stomach Anastomosed to the Jejunum*

Dog	Preoperative Controls				Postoperative Controls				Duration, Days	Ulcer
	Date	Hydrochloric Acid			Date	Hydrochloric Acid				
		Free	Com bined	Total		Free	Com bined	Total		
HH 86	9/ 8/33	16	9	25	10/ 5/33	61	25	86	69	None
	9/12/33	0	64	64	10/13/33	22	16	38		
					10/19/33	50	35	85		
					10/27/33	45	15	60		
					11/ 2/33	30	10	40		
					11/10/33	50	18	68		
					11/16/33	45	49	94		
					11/24/33	49	15	64		
					12/ 1/33	60	20	80		
					12/ 8/33	42	9	51		
					12/14/33	35	80	115		
					12/22/33	67	32	99		
					12/28/33	0	87	87		
					1/ 5/34	60	21	81		
					1/11/34	0	82	82*		
HH 87	9/ 8/33	10	10	20	10/ 5/33	0	5	5*	81	None
	9/12/33	5	10	15	10/13/33	15	5	20		
					10/19/33	14	8	22		
					10/27/33	0	63	63*		
					11/ 2/33	5	5	10		
					11/10/33	10	5	15		
					11/16/33	0	60	60		
					11/24/33	10	20	30		
					12/ 1/33	27	24	51		
					12/ 8/33	5	20	25		
					12/14/33	37	15	52		
					12/22/33	7	4	11		
					12/28/33	5	6	11		
					1/ 5/34	23	19	42		
					1/11/34	10	10	20		
					1/19/34	12	5	17		
HH 88	9/ 8/33	0	5	5	10/ 5/33	81	14	95	152	Ulcers of jejunum
	9/12/33	0	75	75	10/13/33	18	12	30		
					10/19/33	55	21	76		
					10/27/33	30	10	40		
					11/ 2/33	15	10	25		
					11/10/33	33	16	49		
					11/16/33	25	18	43		
					11/24/33	65	24	89		
					12/ 1/33	18	37	55		
					12/ 8/33	35	19	54		
					12/14/33	52	13	65		
					12/22/33	23	15	38		
					12/28/33	5	46	51		
					1/ 5/34	83	10	93		
					1/11/34	83	11	94		
					1/19/34	11	27	38		
					1/25/34	9	43	52*		
					2/ 2/34	0	52	52†		
					2/ 8/34	4	8	12		
					2/16/34	35	22	57		
					2/22/34	50	13	63		
HH 77	9/ 7/33	20	22	42	Died 9/19/33 during rest period, 8 days postoperatively					Hemorrhagic erosions perforated marginal ulcer
	9/ 8/33	14	17	31						

\* Mucus

† Food

accustomed to receive acid gastric chyme and not possessing sufficient inherent resistance to withstand the action of the gastric juice, is digested, with the resultant development of a chronic ulcer. In these experiments the susceptibility of the tissue to ulceration was demonstrated. Of the 7 dogs in which the pouch of the lesser curvature was anastomosed to the jejunum, 3 were given injections of histamine, and ulcers developed in all (100 per cent). Of 4 control animals not receiving histamine, ulcers developed in only 2 (50 per cent). The results obtained in these dogs with pouches of the lesser curvature illustrate the rôle which acidity plays in the production of ulceration, since of the animals receiving histamine ulcers developed in all (100 per cent), whereas of the control group in which histamine was not used ulcers developed in only 50 per cent. The significance of acidity in the development of ulceration was also demonstrated in experiment 3, in which the pouch from the greater or the lesser curvature of the stomach was anastomosed to the jejunum, as follows. In all the 6 animals in which the pouch of the greater curvature was anastomosed to the jejunum ulcers developed, whereas ulcers developed in 5 (71 per cent) of the 7 animals in which the pouch of the lesser curvature was anastomosed to the jejunum. In both of these groups the sensitivity of the jejunal mucosa is presumably the same, the difference in the incidence of ulcers probably being due to the relatively higher acidity in the animals with anastomosis of the pouch of the greater curvature. As mentioned earlier, the gastric acidity is derived largely from the fundus and greater curvature of the stomach, so that the secretion from the pouch of the greater curvature should be greater, with higher values for acid, than that from the pouch of the lesser curvature.

The importance of the neutralization of acidity in the protection of the intestinal mucosa from the digestive action of gastric juice is illustrated by the results obtained in experiment 4, in which pouches from the greater and the lesser curvature of the stomach were anastomosed to the jejunum and the gallbladder. In this experiment the same conditions prevailed as in experiment 3, with the exception that alkaline bile was introduced into the pouch by anastomosing the gallbladder and ligating the common duct. The protective influence of the alkaline bile was demonstrated by the fact that of the 6 animals in which the pouch of the lesser curvature was used ulcers developed in only 3 (50 per cent), as contrasted with the 71 per cent incidence of ulcers in the dogs with a pouch of the lesser curvature in experiment 3, in which the alkaline bile was not present. Of the 7 animals in experiment 4 in which the pouch of the greater curvature was anastomosed to the jejunum and gallbladder, ulcers developed in only 2 (28 per cent), as contrasted with the 100 per cent incidence of ulcers in the animals with a pouch of the

In the experiments with the pouch of the lesser curvature (modified Pavlov type) with jejunal anastomosis (thus simulating Meckel's diverticulum containing gastric mucosa) chronic jejunal ulcers were present in all 3 dogs that received histamine and no jejunal ulcers were present in 2 of 4 control dogs that did not receive histamine (tables 10 and 11). In the experiments on the lesser curvature with jejunal anastomosis there were seven jejunal ulcers four of which were located in the efferent loop of the jejunum two opposite the stoma and one at the margin. Two of the ulcers in the efferent loop (HH 83 and 93) and one marginal ulcer (HH 77) perforated (fig. 8). The two jejunal ulcers shown in figure 9, showed healing which was verified microscopically. This series of experi-

TABLE 12—*The Effect of Ulcers in Animals with Modified Heidenhain Pouch of the Greater Curvature of the Stomach Anastomosed to the Jejunum and the Gallbladder Following the Administration of Histamine Subcutaneous, the Bile Acting as a Buffer to the Hydrochloric Acid in the Pouch*

Dog	Acidity Before Injections of Histamine				Acidity After Injections of Histamine				Duration of Days	Ulcer
	Date	Hydrochloric Acid			Date	Hydrochloric Acid				
		Free	Combined	Total		Free	Combined	Total		
HH 64	1 12 '33	22	17	39	2 5 '33	6	5	11	11	Hemorrhages
	1 15 '33	27	18	45	2 6 '33	10	6	16		
					2 17 '33	10	10	20		
					2 20 '33	31	20	51		
HH 65	7 25 '33	18	12	30	8 11 '33	14	27	41	27	None
	7 27 '33	23	16	39	8 15 '33	6	27	33		
					8 25 '33	-	28	28		
HH 73	8 25 '33	27	18	45	9 15 '33	37	27	64	25	Ulcers of jejunum perforated jejuna ulcer
	8 28 '33	16	23	39	9 21 '33	27	11	38		
HH 76	8 29 '33	0	20	20	9 21 '33	0	15	15	127	Ulcers of jejunum
	8 31 '33	0	16	16	9 22 '33	0	15	15		
					10 1 '33	0	16	16		
					10 12 '33	26	20	46		
					10 17 '33	51	0	51		
					10 27 '33	4	15	19		
					11 2 '33	6	20	26		
					11 16 '33	5	12	17		
					11 1 '33	5	21	26		
					11 2 '33	27	18	45		
					12 1 '33	14	21	35		
					12 8 '33	23	10	33		
					12 14 '33	15	0	15		
					12 22 '33	25	5	30		
					12 29 '33	21	5	26		
					1 '34	18	10	28		
					1 11 '34	0	17	17		

ments in which Meckel's diverticulum containing gastric mucosa was simulated showed that an unneutralized acid secretion flowing into the jejunum usually not accustomed to being bathed in such an acid fluid, may cause true ulcers on the jejunal mucosa. It confirms the clinical observation that the presence of gastric mucosa in Meckel's diverticulum may lead to ulceration of the intestinal mucosa.

EXPERIMENT 4—*Observations on dogs with the pouch of the gallbladder anastomosed to (a) the Heidenhain pouch (fig. 4) or (b) the Pavlov pouch (fig. 5)*

A pouch of the greater curvature (Heidenhain pouch) with anastomoses to the jejunum and gallbladder was made in 25 dogs. 7 of which lived long enough for completion of observations (tables 12 and 13). A pouch of the lesser curva-



greater curvature in experiment 3, in which the bile was not present. The relatively greater protection in the animals with a pouch of the greater curvature in experiments 3 and 4 when bile was present was probably due to the greater neutralization of a previously higher acidity. The relative protective influence of bile in the pouch of the animals with a lesser curvature was comparatively less than in the animals with a pouch of the greater curvature, probably because in the former the acidity was not so high, so that the neutralization played a less important rôle. The fact that ulcers developed in 50 per cent of the animals with a pouch of the lesser curvature and anastomoses to the jejunum and gallbladder, as compared with 28 per cent of a similar series in which the pouch of the greater curvature was used is interesting. The higher incidence in the former group may have been due to the increased secretion, the result of intact nerve supply.

From our clinical observations<sup>58</sup> and the results obtained in the present investigation, we are of the opinion that there are three factors operative in the production of peptic ulcer: (1) predisposition (ulcer diathesis), which is inherent in certain persons, (2) susceptibility of the tissue and (3) hyperacidity. In the experimental animal ulcer diathesis is known not to occur because ulcers are rarely found in dogs, so that the present investigation was concerned chiefly with susceptibility of the tissue and hyperacidity. As shown in the experiments with extirpation of the gastric curvatures, the lesser curvature of the stomach is more susceptible to ulceration than are other portions. Similarly, anastomoses between the pouches of the curvatures and the jejunum, with the high incidence of ulceration in the jejunum, demonstrate the susceptibility of the jejunal mucosa to peptic ulceration. The rôle of acidity was illustrated in the present investigation (1) by the development of ulcers in normal animals receiving either hydrochloric acid by mouth or injections of histamine, (2) by the high incidence of ulcers of the jejunum when the pouches of the lesser and greater curvatures were anastomosed to the jejunum, and (3) by the relatively lower incidence of jejunal ulcer when neutralization of the acid gastric chyme by bile was accomplished in those animals with anastomoses to the gallbladder.

#### SUMMARY

An investigation to determine the role of tissue susceptibility and hyperacidity in the formation of ulcers is reported. A total of 125 dogs was used, but only 56 animals survived sufficiently long to provide adequate observations.

<sup>58</sup> In a subsequent article the clinical application of the experimental findings is to be reported.

(Pavlov) with anastomoses to the jejunum and gallbladder was made in 18 animals, of which only 6 lived sufficiently long for completion of observations (tables 14 and 15) Bile prevented the postoperative anastomotic ulcer from forming in the 3 dogs with the Heidenhain pouch in which the jejunum and the gallbladder had been anastomosed, but it did not prevent the formation of chronic anasto-

TABLE 13—*Incidence of Ulcers in Control Animals with Modified Heidenhain Pouch of the Greater Curvature of the Stomach Anastomosed to the Jejunum and Gallbladder*

Dog	Preoperative Controls				Postoperative Controls				Dura- tion, Days	Ulcer			
	Date	H <sub>3</sub> drochloric Acid			Date	Hydrochloric Acid							
		Free	Com bined	Total		Free	Com bined	Total					
HH 59	6/23/32	20	14	34	7/ 8/32	0	5	5*	112	Hemorrhages of stomach erosions of stomach			
	6/24/32	21	14	35	7/14/32	5	25	30					
					7/22/32	5	16	21					
					7/26/32	25	22	47					
					8/ 5/32	10	13	23					
					8/19/32	34	14	48					
					8/25/32	33	17	50					
					9/ 2/32	0	17	17					
					9/ 8/32	0	44	44					
					9/22/32	0	73	73					
					10/ 1/32	16	12	28					
					10/ 6/32	23	16	39					
					10/14/32	18	14	32					
					10/21/32	12	14	26					
HH 70	2/23/33	22	8	30	5/12/33	12	12	24	81	Gastritis			
					5/18/33	29	22	51					
					5/26/33	64	31	95					
					6/ 1/33	76	20	96					
					6/ 9/33	80	6	86					
					6/15/33	59	19	78					
					6/23/33	40	6	46					
					6/29/33	39	14	53					
					7/ 7/33	40	60	100					
					7/13/33	52	20	72					
					7/22/33	45	20	65					
	HH 68	1/27/33	0	12	12	2/23/33	57	13			70	160	Gastritis
		2/ 3/33	40	5	45	3/ 5/33	15	5			20		
						3/ 8/33	0	22			22*		
					3/17/33	0	30	30*					
					3/23/33	13	22	35					
					3/31/33	0	46	46					
					4/ 6/33	53	32	90					
					4/20/33	0	34	34					
					4/28/33	23	27	50					
					5/ 4/33	14	31	45					
					5/12/33	0	55	55					
					5/18/33	46	19	65					
					5/26/33	32	28	60					
					6/ 1/33	14	16	30					
					6/ 9/33	0	40	40					
					6/15/33	6	17	23					
					6/23/33	26	12	38					
					6/29/33	0	47	47					
					7/ 7/33	0	29	29					
					7/13/33	15	10	25					
					7/22/33	14	8	22					
					7/27/33	15	8	23					

\* Mucus

motie ulcer after stimulation with histamine in 2 (HH 75 and 76) of the 4 dogs that received histamine There were three jejunal ulcers in the 2 dogs, one each in the afferent and the efferent loop of the jejunum and one opposite the gastrojejunal stoma (fig 10) It was the ulcer in the efferent loop that perforated In both of these animals the stimulation with histamine produced high values for acidity as compared with the preoperative values All 7 dogs

In the first experiment hydrochloric acid was administered by mouth or histamine was injected subcutaneously. Erosions or ulcers developed in 27 per cent of the animals.

In the second experiment, either the lesser or the greater curvature of the stomach was extirpated. Of the animals in which the greater curvature was removed, leaving the lesser curvature in situ, ulcers developed in 63.6 per cent, as contrasted with the group in which the lesser curvature was removed, leaving the greater curvature in situ, in which ulcers did not develop. This presumably was due to the greater susceptibility of the lesser curvature of the stomach to the acid gastric chyme.

In the third experiment, a gastric pouch was made from the lesser or the greater curvature and anastomosed to the jejunum. Of the animals in which a pouch was formed of the lesser curvature jejunal ulcers developed in 71 per cent, whereas of those in which a pouch was formed of the greater curvature ulcers developed in 100 per cent. The high incidence of ulceration in this group was undoubtedly due to the susceptibility of the tissue of the jejunum to the acid gastric chyme.

In the fourth experiment, a gastric pouch was made from the greater or the lesser curvature of the stomach and anastomosed to the jejunum and gallbladder. The incidence of jejunal ulcers was 50 per cent in dogs with a pouch of the lesser curvature and 28 per cent in those with a pouch of the greater curvature. The reduction in acidity in this group was undoubtedly responsible for the decreased incidence of ulcers as compared with that in experiment 3, in which there was absence of bile.

On the basis of our clinical observations and the results obtained in the present investigation, we believe that the factors responsible for the production and persistence of peptic ulcer are as follows: (1) predisposition to ulcer (ulcer diathesis), (2) susceptibility of the tissue and (3) hyperacidity. The therapy in cases of peptic ulcer should consist largely of minimizing susceptibility of the tissue by not performing gastro-enterostomy on patients with normal acidity or hyperacidity, and by using those measures which will decrease gastric acidity.

TABLE 14—*Incidence of Ulcers in Animals with a Modified Pavlov Pouch of the Lesser Curvature of the Stomach Anastomosed to the Jejunum and the Gallbladder Following the Subcutaneous Administration of Histamine*

Dog	Date	Acidity Before Injections of Histamine			Acidity After Injections of Histamine				Dura- tion, Days	Ulcer
		Hydrochloric Acid			Hydrochloric Acid					
		Free	Com- bined	Total	Date	Free	Com- bined	Total		
HH 87	9/ 8/33	10	10	20	2/ 2/34	23	9	32	62	None
	9/12/33	5	10	15	2/ 6/34	25	10	35		
					2/ 8/34	48	15	63		
					2/16/34	59	14	73*		
					2/22/34	40	9	49		
					3/ 2/34	18	24	42		
HH 118	11/30/33	14	14	28	1/25/34	5	36	41	61	None
	12/ 8/33	14	6	20	2/ 1/34	4	12	16		
	12/28/33	19	22	41	2/ 8/34	14	10	24		
					2/16/34	18	4	22		
	Postoperative values				2/22/34	8	10	18		
	1/24/34	8	14	22	3/ 2/34	5	5	10		
HH 121	12/21/33	8	7	15	1/25/34	50	16	66	23	None
	12/22/33	8	12	20	2/ 2/34	33	11	44		
	Postoperative values				2/ 8/34	57	14	71		
	1/23/34	14	11	25	2/16/34	58	14	72		

\* Bile

TABLE 15—*Incidence of Ulcers in Control Animals with a Modified Pavlov Pouch of the Lesser Curvature of the Stomach Anastomosed to the Jejunum and the Gallbladder*

Dog	Date	Preoperative Controls			Postoperative Controls				Dura- tion, Days	Uleer
		Hydrochloric Acid			Hydrochloric Acid					
		Free	Com- bined	Total	Date	Free	Com- bined	Total		
HH 106	11/ 9/33	20	18	38	12/15/33	5	7	12	50	Marginal ulcer perforated jejunal ulcer
	11/10/33	10	5	15	12/22/33	5	70	75		
					1/ 5/34	0	87	87		
					1/19/34	12	29	41		
HH 113	12/ 1/33	10	5	15	Died 1/5/34 during rest period, 10 days postoperatively					Perforated marginal ulcer duodenal ulcer
	12/ 8/33	27	22	49						
HH 120	12/21/33	15	6	21	1/23/34	50	11	61	49	Frosion <sup>c</sup> ulcers and hemorrhages of stomach ulcer of jejunum
					1/25/34	8	35	43*		
					2/ 2/34	50	21	51		
					2/ 8/34	8	4	12		
					2/16/34	21	11	32		
					2/22/34	57	35	92		

\* Mucus

# THE ACETABULAR INDEX IN INFANTS IN RELATION TO CONGENITAL DISLOCATION OF THE HIP

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It is axiomatic that prevention is more valuable than cure. The practice of this principle is nowhere more desirable than in the management of congenital dislocation of the hip. This common lesion has been studied carefully for decades by hundreds of surgeons all over the world with the result that its pathologic process is thoroughly appreciated, and success in its treatment is readily obtainable, yet there is no one established system but a diversity of methods, even when the treatment is applied during infancy. When the condition continues to childhood or early adolescence, not to speak of adult life, without recognition or adequate treatment, then treatment by any method aims only for improvement in ambulation and for some measure of stability of the hip. So it was like a refreshing breeze on a hot summer day to listen to Dr. Putti, in July 1929 in London, expounding his theory of the possibility of recognizing potential dislocation of the hip during the early months of life and of the ease with which the normal relationship of the osseous elements of the hip can be established and assured.

The recognition during the early months of life of the existence of maldevelopment in the structures of the hip, especially the bony parts, likely to eventuate in a dislocation, depends on the appreciation of the differences between the normal and the abnormal roentgenographic appearance of this joint. It has been abundantly emphasized that in congenital dislocations there is, in addition to a poorly developed or anteverted femoral head and neck, a shallow acetabulum, with the roof, or iliac segment abnormally oblique or even nearly vertical, giving diminished or no resistance to upward displacement of the femur. It occurred to one of us (S. K.) in an examination of a large number of new-born infants, that it might be possible, by study of the angle of inclination of the iliac segment (roof) of the acetabulum with the horizontal line in normal and in congenitally dislocated hips, to arrive at some practical basis of measurement which would help to determine in the new-born whether the hips are normal or are likely to become dislocated. As the obliquity of the acetabular roof is always marked

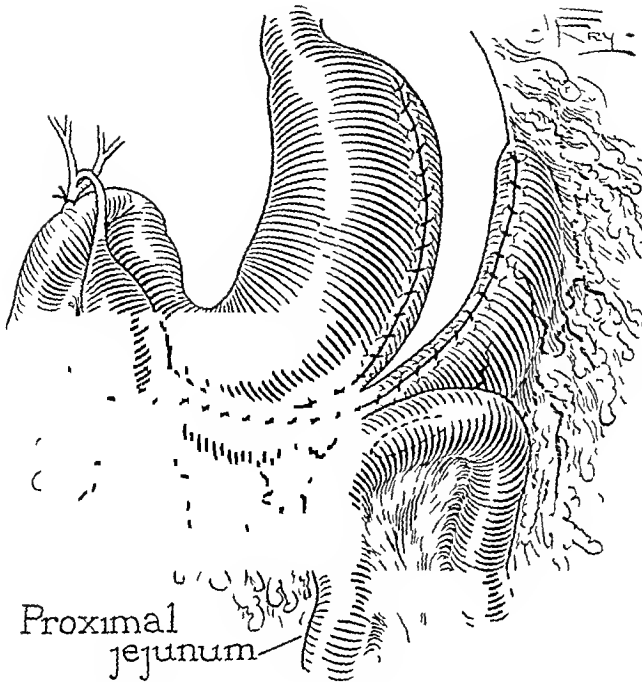


Fig 4—A drawing showing the formation of a gastric pouch from the greater curvature and anastomosis of the proximal jejunal loop and fundus of the gallbladder to this pouch The common bile duct is sectioned and doubly ligated

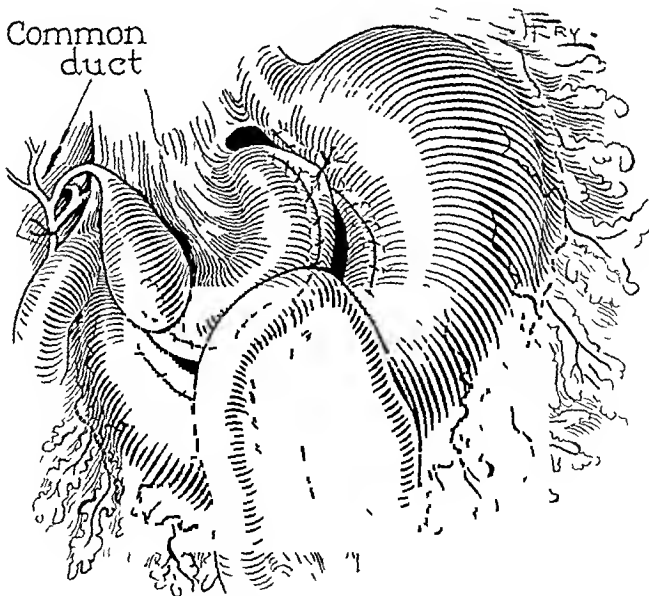


Fig 5—A drawing showing the formation of a gastric pouch from the lesser curvature and anastomosis of the proximal jejunum and fundus of the gallbladder to this pouch The common bile duct is sectioned and doubly ligated

in dislocated hips and is regularly slight in normal hips, we concluded that the angle of inclination of the acetabular roof with the horizontal line would be the most serviceable means of judging the normality or abnormality of a hip joint relative to a possible appearance of a dislocation. This angle we shall call, for purposes of convenience, the acetabular index. We have investigated the acetabular index of hips in normal children at birth and at about 2 years of age and in those with congenital dislocations and herein present the results of our study and the conclusions drawn from them.

Twenty-three normal infants, varying in age from 1 to 7 days, were examined and roentgenograms were made of their pelvis. Table 1 gives our observations. The acetabular angle, or index, varied between 25 and 32 degrees, the average being 27.5. There was no appreciable difference in the indexes of the right and left hips, nor was there any marked disparity in the indexes of the two sexes. Figure 1 is a tracing of the roentgenogram of the hips of one of these infants, with an acetabular index of 25 degrees.

As most of the infants with congenital dislocation in this country come under observation when they are between 1½ and 2 years old, we next studied the hips of a group of twenty normal children varying in age between 11 and 24 months. Table 2 shows that the average acetabular index in these forty hips was 20 degrees, considerably lower than that in the new-born infants. Figure 2 is a tracing of the hips of a child in this group. The method of mensuration is obvious. A horizontal line is drawn between the triradiate cartilages. A line is then drawn from the upper pole of the acetabulum to the point of contact of the iliac segment of the acetabulum with the triradiate cartilage, forming an angle with the horizontal line. The resultant angle, or acetabular index, reveals the relative depth of the socket of this hip joint and is an index of the resistance which the iliac portion of the acetabulum would present to luxation of the head of the femur. We appreciate that there are many additional factors, such as the thickness of the cotyloid ligament, the conformation and distribution of the capsule of the hip, the size and shape of the head of the femur, the degree of torsion in the neck of the femur and so forth, which influence the development of a dislocation. But the angle of the roof of the acetabulum with the horizontal line, that is, the acetabular index, affords a ready and, we believe, a reliable means of visualizing the future osseous structure of the acetabulum in relation to the head of the femur and aids in deciding whether a dislocation will or will not occur. A high acetabular index warns that a dislocation will or may appear and offers the opportunity of instituting preventive measures, which, from Putti's reports, are eminently successful.



Fig 6 (dog HH 43)—Histamine was injected three times daily on alternate days for a period of one hundred and thirty-four days. The stomach was opened along the greater curvature. The pyloric regions and the duodenum were pale in comparison with the fundus which was markedly injected. Note that most of the erosions and acute ulcerations are in the pyloric antrum. About twenty-two acute ulcers can be counted.

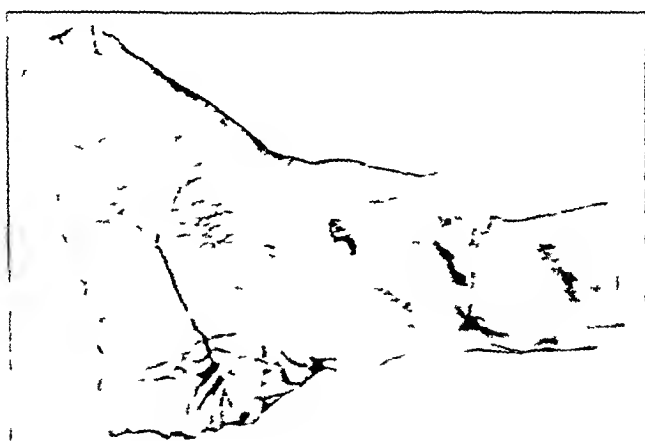


Fig 7 (dog HH 52)—A control animal observed for fourteen days post-operatively. The anastomosis between the gastric pouch and jejunum has been cut open. On the jejunal side there is a large ulceration in the center of an extensive ulceration.



TABLE 1—Acetabular Indexes for New-Born Infants \*

Patient No	Sex	Acetabular Index, Degrees	
		Right Hip	Left Hip
1	M	32	31
2	F	31	30
3	F	28	30
4	M	29	30
5	M	27	25
6	F	30	22
7	F	25	25
8	M	26	25
9	F	25	27
10	F	30	26
11	F	28	28
12	M	27	27
13	M	28	28
14	F	27	28
15	M	25	27
16	F	25	25
17	M	25	25
18	M	25	27
19	F	28	22
20	M	29	27
21	F	26	27
22	F	27	28
23	M	28	30
Pecume		Acetabular Index, Degrees	
Sex		Right Hip	Left Hip
12 F		27	28
11 M		27	27
Average		Acetabular Index, Degrees	
Lowest angle		27.5	
Highest angle		25	
		25	

\* These infants were examined in the maternity ward of the Israel Zion Hospital Brooklyn

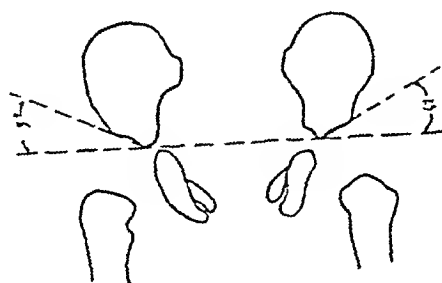


Fig 1—The hips of a normal infant at birth

We next examined the roentgenograms of thirty-five congenitally dislocated hips in children from 12 to 36 months of age. All these children had been treated at the Hospital for Joint Diseases. The average acetabular index was 37.5 degrees (table 3) as compared with an average of 20 degrees for normal children of the same age (table 2) and 27.5 degrees for the new-born (table 1). The difference in the acetabular indexes of normal and congenitally dislocated hips is striking and is graphically represented in figure 3 which is a tracing of the pelvis of a patient in this group (patient 8) who had a congenital

in this group had a mild to moderate jejunitis of the efferent loop in spite of the more or less neutralizing effect of the bile. In the 3 dogs with a modified Pavlov pouch in which no histamine was used bile flowing through the anastomosis did not prevent the formation of jejunal ulcers. There was a total of four ulcers, one acute and three chronic. As regards location, two were in the margin, one in the efferent loop and one opposite the stoma. The ulcers in 2 of these animals (HH 106 and 113) perforated (fig 11). The greater secretory activity of this Pavlov type of pouch because of its intact vagal nerve supply may be surmised to be one factor in the production of ulceration in some instances. As regards the lesions of the stomach or duodenum itself, deviation of the bile toward the pouch in 13 dogs produced hemorrhages and erosions of the main portion of the stomach in only 1 animal (HH 120), a duodenal ulcer in another (HH 113) and a small pyloric mucosal hemorrhage in 1 that received histamine.

#### COMMENT

*Gastric Ulceration*—It is significant in the experiments on extirpation of the curvature that the incidence of ulceration and erosion in the lesser curvature after the extirpation of the greater curvature was 63.6 per cent, whereas no ulcers or erosions occurred in the remaining greater curvature after extirpation of the lesser curvature. These facts, together with the observation that following the injection of histamine multiple ulcers occurred most frequently along the lesser curvature (HH 43, fig 1), support the clinical observations that gastric ulcer occurs generally along the lesser curvature (Magenstrasse). If the formation of ulcer were the result of mechanical injury of the mucosa by the motor activity of the stomach and impingement of food against the lesser curvature, the incidence of ulceration following extirpation of the lesser curvature should have been as high as that following extirpation of the greater curvature. The fact that no ulcers occurred in the dogs subjected to the former procedure and that ulcers and erosions developed in 63.6 per cent of the group on which the latter operation was performed suggests that susceptibility of the tissue of the original lesser curvature predisposed to ulceration. On the basis of experiments 1 and 2, in which acute ulcers were obtained in 27 per cent of the dogs after feeding of 1 per cent hydrochloric acid or stimulation with histamine, one is justified in inferring that gastric acidity is a probable factor in the etiology of peptic ulceration. As these were normal animals, the high incidence of ulceration is even more noteworthy, in spite of the fact that the degree of acidity obtained is probably higher than ever occurs in normal human beings. In the human patient with ulcer, however, there exists an ulcer diathesis, in that the patient's predisposition to ulceration is inherent, and his gastric and duodenal mucosa is probably abnormally sensitive to the digestive action of acid gastric juice. The abnormal sensitivity of mucosa to peptic ulceration was

TABLE 2—*Acetabular Indexes of Normal Hips in Early Childhood*

Patient No	Age in Months	Acetabular Index, Degrees	
		Right Hip	Left Hip
1	24	21	21
2	24	19	22
3	21	22	22
4	17	21	21
5	16	20	22
6	24	19	19
7	24	19	19
8	24	18	18
9	23	22	20
10	20	19	20
11	24	18	18
12	24	18	18
13	12	21	20
14	20	23	24
15	12	20	20
16	12	20	21
17	11	18	20
18	24	19	20
19	19	25	21
20	18	22	22
Resumé			
Total number of normal hips		40	
Average age		19 mo	
Youngest		11 mo	
Oldest		24 mo	
		Acetabular Index Degrees	
Average		20	
Lowest angle		18	
Highest angle		25	

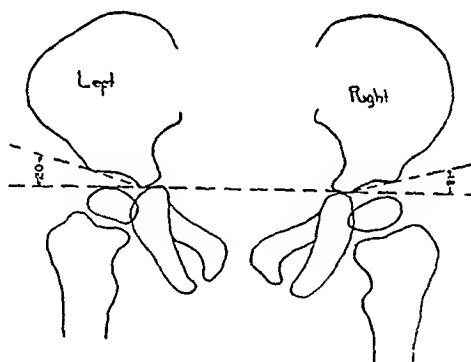


Fig 2—The hips of a normal infant at the age of 17 months

dislocation of the left hip. The acetabular index of the left hip was 38 degrees, while that of the right, or normal hip, was only 22 degrees.

Putti, in describing a method of roentgenologic examination of infants in what he called the preslipping state, classified hips into those with horizontal, obtuse or right angles, depending on the general inclination of the superior, or iliac, segment of the acetabulum. In our investigation we sought more accurate information aiming to establish, if possible, a constant for the normal infant and thus to be enabled more readily to diagnose the abnormal. From our study we can state that an acetabular index above 30 degrees foreshadows a possible dislocation of the hip.

# POSTANESTHETIC HEADACHE

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MUSCAT, ARABIA

There are three possible methods of anesthesia. One can anesthetize sensory nerve endings so that their stimulation gives rise to no afferent impulses. One can interrupt the transmission of afferent impulses by anesthetizing the nerve trunks which carry them. And finally one can stupefy the entire organism so that afferent impulses fail to register on arrival at the higher centers.

Anesthetization of the sensory endings has the advantage of safety, but for the patient it makes surgical procedure a harrowing experience, and the capacity of the tissues to heal is lowered by the necessary infiltration with fluid. The disadvantages of a general intoxication so profound that the higher centers are incapable of reacting to afferent impulses require no discussion.

Theoretically conduction anesthesia is much the best. There is no general intoxication, and no injury to the tissues involved in the operation. Spinal anesthesia is the ideal conduction method. In the subarachnoid space the sensory nerves are assembled in a beautifully convenient way. If one were able to avoid the complicating factors spinal anesthesia would long since have displaced every other method.

The complicating factors have not been avoided. Cerebral anemia and respiratory paralysis have caused death in many cases, and at the moment spinal anesthesia is the most dangerous method in common use. But the discussion of these catastrophes has obscured the fact that for operations below the umbilicus spinal anesthesia, far from being excessively dangerous, is perhaps the safest method, and in comfort to the patient and convenience to the surgeon is almost ideal. Anesthetization of the point of spinal puncture makes the procedure practically painless for the patient, and recollection that heavy solutions gravitate downward makes the method safe. If the Trendelenburg position is wanted a heavy solution must not be used, and procaine crystals dissolved in spinal fluid form a heavy solution.

But an anesthetic must do more than furnish a satisfactory period for the execution of some surgical procedure. It must leave the patient undisturbed and comfortable after the operation is over. Spinal anesthesia has a bad record on this point. Postanesthetic headache has occurred frequently, and sometimes has been very severe. The dangers from a poorly given general anesthesia are much more serious than the discomfort of an occasional severe headache, but when the comparison

is made with the effects of ether expertly given, the headache may be sufficient to throw the whole method of spinal anesthesia into the discard. On the other hand, if the postanesthetic headache can be eliminated, for operations below the umbilicus spinal anesthesia stands in a class by itself.

Not much progress has been made in dealing with the problem of headache. It is difficult to investigate. There is a widespread impression that continued leakage from the puncture hole sometimes occurs and that this leakage by reducing the pressure within the subarachnoid space causes the headache. This may have been true once, when shockingly coarse needles were used even for routine diagnostic punctures. Fine delicate needles are used universally now, and the headache remains. The holes made by such delicate needles must be studied with a magnifying glass. They are tiny slits the edges of which automatically approximate on withdrawal of the needle, and it is impossible to believe that they permit any significant leakage, at least for any great length of time.

Regarding some other possible causes of headache there is more certainty. Postanesthetic headache will occur if the injected solution is irritating. Wayne Babcock,<sup>1</sup> the dean of the spinal anesthetic faculty, reported his experience with defective distilled water. Headache occurred frequently until this fault was corrected. I have seen the same thing in Muscat. Old rubber tubing in the distilling plant caused postanesthetic headache which for frequency and severity I have not seen equaled since. The fault was corrected, and the incidence of headache dropped to its former figure. A few months ago the solution which had caused almost no trouble in Muscat was reported as causing many headaches in a neighboring clinic. I found that spinal puncture was being made through skin dripping with tincture of iodine.

This matter of the irritating character of the anesthetic has not received the attention that it deserves. Any one of several factors can make such a solution irritating. In the first place, it may be irritating because of the chemicals it contains. Stovaine has enjoyed a great vogue as a spinal anesthetic, but it is highly unsuitable, being much more irritating than procaine hydrochloride.<sup>2</sup> In the second place, an acid solution is irritating. Any solution injected into the subarachnoid space should have a  $p_H$  above 7 and not below. That was the fault of the solution which caused so many headaches in Muscat. It was strongly acid. In the third place, a solution which is either hypertonic or hypotonic is irritating. That is probably the reason that procaine

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1 Babcock, Wayne. Surg, Gynec & Obst 59 94 (July) 1934

2 Braun, H. Lokalanesthetie, ed 3, Leipzig, Johann Ambrosius Barth, 1914, p 133

TABLE 3—Acetabular Indices of Congenital Dislocated Hips in Early Childhood

Patient No	Acetabular Index, Degrees		
	Age in Months	Right Hip	Left Hip
1	24	42*	20
2	22	45*	30*
3	16	20	40*
4	36	20	38*
5	36	20	42*
6	16	25	40*
7	14	46*	40*
8	18	22	35*
9	12	34*	25
10	36	34*	38*
11	16	18	28*
12	18	20	33*
13	36	20	41*
14	20	18	48*
15	30	39*	48*
16	19	40*	49*
17	21	32*	38*
18	18	27	35*
19	20	40*	24
20	21	33*	33*
21	24	35*	35*
22	27	30*	28*
23	24	28*	20
24	18	35*	20
25	18	20	28*
Resume			
Total number of congenital dislocated hips		75	
Average age		22 mo	
Youngest		12 mo	
Oldest		36 mo	
Acetabular Index, Degrees			
14 Right hips		37	
21 Left hips		38	
35 Combined hips		37.5	

\* Dislocated hip

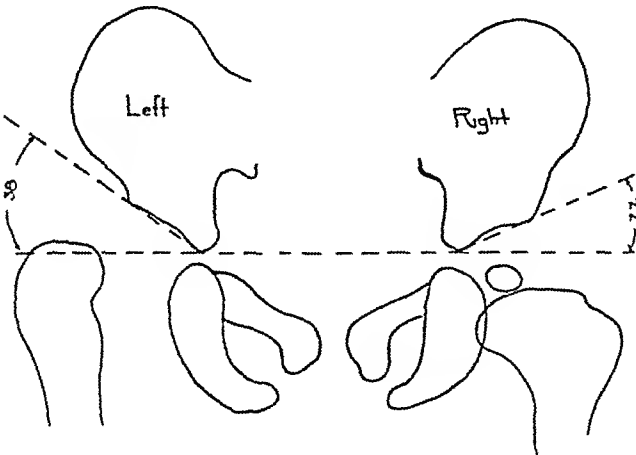


Fig 3—Congenital dislocation of the left hip in an infant of 18 months

Serious symptoms were noted for several weeks, and the animal remained prone. Jaundice was severe, and the stool was bloody for a few days. Gradual improvement occurred. Five weeks after operation the animal was again in good condition.

On December 10 the animal was electrocuted. Postmortem examination showed that the general condition was good. Jaundice was slight. Extensive adhesions were noted between the liver and the duodenum. The bile ducts were slightly

TABLE 1—Results of the Bacteriologic Examination of the Bile

Group	Dog No	Duration of Life	First Period, 2 to 20 Days	Second Period 29 to 41 Days		Third Period, 4½ to 5½ Months	
				4 Weeks After First Operation			
				Bacteria Present	Bacteria Injected	Bacteria Found Post Mortem	
1	789	2 days	Str haemo-lyticus, B coli, B Welchii				
	990	5 days	Str haemo-lyticus, B Welchii				
	771	11 days	B coli, B Welchii				
	886	20 days	Staph aureus, B Welchii				
2	792	29 days		Gram positive rod, B coli	B coli	B coli, streptococcus gram positive rod shaped bacteria	
	768	32 days		Str haemo-lyticus	Staph aureus	Str haemo-lyticus Staph aureus B Welchii	
	728	41 days		Sterile	Staph aureus	Staph aureus	
3	415	5½ mo		Sterile	Staph aureus		
	772	4½ mo		Staph albus	B coli		
	789	4½ mo		Sterile	B coli		
	991 Control	4½ mo					
						After Electrocution	
						Bacteria	Bile
						Str haemo-lyticus, B Welchii	White
						B coli	White
						B coli diphtheroid bacillus	Almost white
						Staph albus	Deep green

dilated. A hemorrhagic infarct the size of a walnut was present in the spleen. The intestinal mucosa was red and contained mucus. Aspiration yielded 0.5 cc of fluid, which was bloody but not bile-colored.

After the bile had been centrifuged the supernatant fluid was clear. Bacterial culture yielded B coli. Chemical analysis gave negative results for bilirubin. The sediment contained many leukocytes, erythrocytes and amorphous crystals.

Histologic examination of the liver showed marked fatty infiltration, which spared large areas. Pigment was noted in the capillaries but not in the hepatic cells. There was evidence of a little interstitial reaction.

In the matter of the technic of roentgenologic examination of the pelvis it is imperative to observe several important details. The infant should be placed on its back, with the lower limbs in contact and in complete extension at the hip joints, with the patellae facing forward. The roentgen tube must be focused or centered in the midline of the body and directly over the superior border of the symphysis pubis. Deviation from this routine, such as tilting of the pelvis or angulation of the tube, will give distorted views and erroneous measurements. In figure 4 there are tracings of two views of the same pelvis. The position of the pelvis in *A* is correct. In *B* the pelvis is rotated to the right and flexed, with a resultant apparent increase in the right and decrease in the left acetabular index and narrowing of the left triradiate space. Reliable information is obviously dependent on accurate roentgenographic technic.

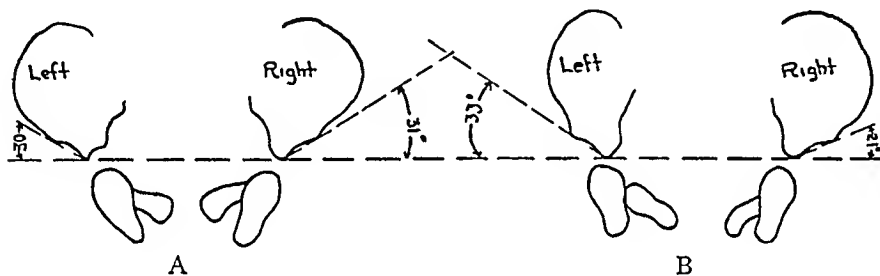


Fig 4—Correct and incorrect views of the same pelvis. *A* is taken from the correct angle. In *B* the pelvis is tilted to the right, resulting in a change in the acetabular index and yielding incorrect information.

#### CONCLUSIONS

- 1 The acetabular index is the angle formed between the roof or iliac portion of the acetabulum and a horizontal line passing through the triradiate cartilages.
- 2 The acetabular index in new-born normal infants is regularly low, the average being 27.5 degrees.
- 3 The acetabular index in normal children about 2 years of age is lower than that in children at birth, with an average of 20 degrees.
- 4 The acetabular index in congenitally dislocated hips of children of about 2 years of age is constantly high, the average being 37.5 degrees.
- 5 In an infant having a high acetabular index, that is, above 30 degrees, a dislocation of the affected hip will probably develop.
- 6 An infant with a high acetabular index should be placed in an apparatus which will hold the lower limbs continuously in marked abduction until the acetabulum and the capital epiphysis have become thoroughly adapted to each other and there is clinical evidence giving reasonable stability.



Dog 991—Ligation of the common duct was performed on August 1. Severe jaundice developed, and the stool was colorless. No marked symptoms were noted.

On December 14 the animal was electrocuted. Postmortem examination showed that the dog was emaciated and severely jaundiced. Adhesions were present between the gallbladder and the duodenum. The gallbladder was distended and the bile ducts were markedly dilated, the common duct being 1.5 cm and the hepatic duct 1 cm in diameter. The intestinal mucous membrane showed no changes. Aspiration of the bile duct and the gallbladder yielded large amounts of thick, dark green bile with the consistency and appearance of tar.

The bile was so thick that it had to be mixed with water for chemical analysis, and the results obtained were questionable. Bacterial culture of the bile yielded *Staph. albus*. Chemical analysis gave the following values: bilirubin, 148 mg, cholesterol, 1186 mg, and bile acids, 9108 mg per hundred cubic centimeters. The sediment contained many leukocytes, a good deal of pigment and amorphous crystals.

Histologic examination of the liver showed little evidence of interstitial reaction. Fatty degeneration was noted in some areas. Pigment was present in the hepatic cells.

The gallbladder was normal.

Dog 768—The first operation, ligation of the common duct, was performed on July 5. Severe jaundice developed, and the stool was colorless. The dog was emaciated and preferred to lie prone. Diarrhea occurred. Severe symptoms were noted for three weeks, and then slight recovery followed.

The second operation was performed on August 2. An extreme degree of jaundice was noted, affecting especially the internal organs and the omentum. Ascites was present. The gallbladder and bile ducts were greatly dilated. Aspiration yielded thin, slightly brownish bile. Two cubic centimeters of a suspension of *Staph. aureus* in saline solution was injected into the wall and cavity of the common duct. Bacterial culture yielded *Str. haemolyticus*.

The postoperative course was severe, and the animal died on August 6.

Postmortem examination showed evidence of purulent peritonitis. Thin, slightly brownish bile with a grossly diminished color content was aspirated. Bacterial culture of the bile yielded *Str. haemolyticus*, *Staph. aureus* and *B. Welchii*. The sediment contained many leukocytes and erythrocytes. No chemical analysis was made.

## RESULTS

White bile was found in all three dogs in group 3. In two of these cases the bile was entirely colorless, while in the third the coloration was so faint that the bile could safely be considered to be white, in accordance with the work of Klose and Wachsmuth<sup>20</sup> who included under this heading bile that still retained a slight amount of coloration. Only one animal (dog 768) in group 2 showed significant results, the bile from this animal being much lighter in color than normally. It was not so dilute that it could be called white bile, but there was a definite tendency in that direction. Chemical analysis gave results that were in accordance with the colorimetric evaluation. The bile from the dogs in group 3 showed a low content of bile constituents. Bilirubin

20 Klose, H., and Wachsmuth, W. *Arch. f. klin. Chir.* **123** 1, 1923.

# PATHOGENESIS OF WHITE BILE

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The character of the bile which is obtained at operation for obstruction of the common bile duct varies greatly. The most characteristic bile obtained is thick and dark green, but occasionally there is found so-called white bile. The type of bile obtained in each instance has prognostic as well as diagnostic significance. The important and fundamental problem related to the diagnosis is to determine the conditions that are responsible for the production of the different types of bile on different occasions. From the standpoint of the prognosis it is of vital importance to determine whether or not the liver is functioning normally when white bile is obtained. That this is still an unsolved problem is apparent when one reads the varying opinions expressed in the German and in the American literature concerning the prognosis. The German writers consider that the prognosis is much more serious when white bile is present. The extent of damage to the liver must be known when white bile is being produced, in order to determine whether or not one may expect the organ to function normally after relief of the obstruction.

The literature on white bile is extensive and is especially confusing owing to the fact that authors vary in their conceptions of white bile. In the present discussion I shall exclude the colorless fluid that is found only in the gallbladder. Likewise, I shall not consider the real white bile that is found in cases in which the hepatic cells during the course of their development were never able to produce bile pigment and from the very beginning secreted a colorless fluid. This condition is possible only in the new-born and is so rare that it need not be included here. This paper will be restricted to a discussion of the white bile that is obtained at operation for obstruction of the common duct. In this regard the white bile that is of special interest to the surgeon may be defined as the colorless fluid that is found in the bile ducts and gallbladder and that is free from all bile constituents except a mucin-like protein. The white bile that is found in cases of certain types of intoxication of the liver, such as phosphorus poisoning, will not be considered here.

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was absent from the bile of dogs 415 and 772 and had an extremely low value (0.99 mg) in dog 789. The cholesterol and bile acids either showed very low values or were absent. These results are graphically represented in tables 1 and 2. A study of the results shown in these tables immediately suggests the rôle played by infection.

It would be easy to prove that infection is responsible for the production of white bile in dogs if one could draw a hard line between infection and noninfection. Theoretically, if the infection theory is correct, an animal with white bile should show clinical symptoms of illness during the period of obstruction and its bile should contain bacteria and many leukocytes. On the other hand, a control animal should not show any clinical signs of infection and there should be green bile containing no bacteria and leukocytes. From the practical standpoint these limits are not sharply defined and the conditions for determining the presence of infection can be only partially fulfilled. The fact that bile is sterile after four or five months does not prove that an animal did not undergo a severe infection some time during that period. Bacteria may have been present at one time and may have disappeared before the time of examination. On the other hand, bile may contain bacteria even though there are no clinical signs of infection. Recent extensive investigations by Andrews<sup>21</sup> have proved the correctness of these statements. The significance of the bacteriologic examinations will be more thoroughly disclosed later in the paper.

Although there are no definite single criteria for determining the presence of infection, one can, by using a combination of these signs, judge whether or not there has been infection. Consequently, I used as diagnostic signs for the presence of infection the following criteria: (1) the clinical picture after operation (postoperative condition course); (2) the bacterial and leukocytic content of the bile obtained four weeks after the operation from the living dog; (3) the bacterial and leukocyte content of the bile post mortem; and (4) the histologic picture of the liver.

The members of group 3 showed the following general characteristics in common: an uneventful course after the first operation; aspiration of sterile bile four weeks later (with the exception of dog 772); a severe course after the second operation; a high content of virulent bacteria in the bile post mortem (*Str. haemolyticus*, *B. coli*) and a high leukocytic content.

These facts show that these animals suffered no ill effects as a result of the first operation. The fact that *Staph. albus* was present in the bile of dog 772 is of little significance, since this organism is rela-

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<sup>21</sup> Andrews, Edmund. Etiology of Gallstones. II. Analysis of Duct Bile from Diseased Livers. *Arch. Surg.* 25: 1081 (Dec.) 1932.

The first definite description of white bile was given in the works of Courvoisier,<sup>1</sup> in 1890. This author emphasized the importance of the colorless fluid found throughout the entire biliary system rather than that found only in the gallbladder.

Kausch<sup>2</sup> and later Quincke and Hoppe-Seyler<sup>3</sup> attacked this problem from the mechanical point of view. They postulated the so-called *Pavacholie* theory, which is, in effect, that the hepatic cells because of excess pressure in the bile ducts direct the bile into the blood stream rather than into the bile ducts.

There followed a series of clinical contributions by various authors (Berg,<sup>4</sup> Kehr<sup>5</sup> and others) who described white bile in connection with their studies on cholelithiasis. The chief contribution made by these authors was their review of the most common causes of obstruction in connection with the appearance of white bile, i. e., tumor, especially carcinoma near Vater's papilla, cholelithiasis, stenosis of the common or hepatic duct, spasm of the sphincter and other conditions.

In contrast with these mechanical theories, there arose the idea that functional secretory processes are responsible for the production of white bile in the bile ducts. In accordance with this view Berg expressed the opinion in 1916 that one may consider hydrops of the bile ducts to be a purely functional disturbance, which can be increased by obstruction of the large bile ducts but which is not exclusively produced by it. In addition, Berg mentioned a special congenital affinity of certain parts of the bile ducts for mucostase, which facilitates the production of white bile. This secretory theory introduced a new idea into the consideration of the production of white bile, which predominated for a long time. Even that explanation was not in accord with many clinical observations, however. Pallin,<sup>6</sup> in his work entitled "Cancer in Ductus Hepatico-choledochus," stated "If one asks why this phenomenon is found only exceptionally, apparently without any rule, one must admit that one does not know anything about it."

Further consideration of the functional secretory theory is found in the works of Rous and McMaster<sup>7</sup> published in 1921. These authors

1 Courvoisier, L. *Casuistisch-statistische Beiträge zur Pathologie und Chirurgie der Gallenwege*, Leipzig, F. C. W. Vogel, 1890.

2 Kausch, W. *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **14** 104, 1904-1905.

3 Quincke and Hoppe-Seyler. *Die Krankheiten der Leber*, in Nothnagel, C. W. H. *Spezielle Pathologie und Therapie*, Vienna, A. Holder, 1899, vol. 18a.

4 Berg, J. *Studien über die Funktion der Gallenwege unter normalen und gewissen abnormen Verhältnissen*, *Acta chir. Scandinav.*, supp. 2, 1922, p. 1.

5 Kehr. *Ergebn. d. inn. Med. u. Kinderh.* **13** 198, 1914.

6 Pallin, G. *Cancer in Ductus Hepatico-choledochus*, Lund, Hakan Ohlssons Boktryckeri, 1919.

7 Rous, Peyton, and McMaster, Philip D. *The Concentrating Activity of the Gallbladder*, *J. Exper. Med.* **34** 47, 1921; *Physiological Causes for the Varied Character of Stasis Bile*, *ibid.* **34** 75, 1921.

TABLE 2—Results of the Bacteriologic Examination of the Bile of Five Dogs

Dog No	First Operation	Second Operation, 4 Weeks After First Operation			Post operative Course	Duration of Life	Color	Bile Obtained Post Mortem					Sediment
		Aspirated Bile		Post operative Course				Chemical Analysis					
		Color	Results of Culture					Bile rubin, Mg per 100 Cc	Cholesterol, Mg per 100 Cc	Bile Acids, Mg per 100 Cc	Bacteria		
415	Ligation of common duct cholecystectomy	Uneventful	Green	Sterile	Staph aureus	Very serious	5½ mo	White				Str haemo lyticus, B Welchii	Many leuko cytes
772	Ligation of common duct, cholecystectomy	Uneventful	Green	Staph albus	B coli	Very serious	4½ mo	White				B coli	Many leuko cytes and erythrocytes
789	Ligation of common duct	Uneventful	Green	Sterile	B coli	Severe for 6 or 8 days	4½ mo	Almost white	0.99	1.9	108.96	B coli, diphtheroid bacillus	Medium number of leukocytes
991 Control	Ligation of common duct	Uneventful					4½ mo	Green	148.00	118.6	910.50	Staph albus	Some leuko cytes
708	Ligation of common duct	Very serious	Between white and green	Str haemo lyticus	Staph aureus	Very serious	72 days	Between white and green				Str haemo lyticus, Staph aureus, B Welchii	Many leuko cytes and erythrocytes

for the first time produced white bile in the experimental animal. As a result of their experiments, which were performed on dogs, monkeys and cats, they stated as their conclusion that the gallbladder concentrates and thickens the bile while the ducts exert an opposite influence, diluting it slightly with a thin secretion of their own. This secretion is colorless and devoid of cholates, in the dog it is almost watery and clear. In an obstructed duct that is separated from the gallbladder or connected with a pathologically changed one such fluid gradually replaces the small amount of bile originally pent up. This is the so-called white bile found by surgeons. In this connection Rous and McMaster distinguished two different systems. In their "white system" the gallbladder is separated from the ducts, and ligation of the common duct results in the production of white bile. In their "green system" the gallbladder maintains its connection with the ducts, and ligation of the common duct results in the production of thickened green bile. These authors found that white bile normally appeared in the white system after nine or ten days, while the longest period of observation on the green system was forty-four days. In their discussion infection was considered as merely incidental, the chief emphasis being placed on the opposite functions of the gallbladder and the bile ducts.

The theory of Rous and McMaster, which seemed creditable enough at the time of its formulation, was weakened by further observations. Berg, in his monograph on the biliary system, expressed the opinion that the underlying cause in the production of white bile is other than obstruction, since obstruction alone in most cases results in the appearance of dark, concentrated bile.

The clinical information on white bile was enriched in 1923 by Judd,<sup>8</sup> who found white bile in nineteen of six hundred and forty-nine cases in which operation was performed on the common or hepatic duct at the Mayo Clinic. One of these cases, in which the bile changed to green immediately after removal of a stone from the common duct, is of special interest with regard to the problem of hepatic function and its relation to the production of white bile.

Clinical observations on relief of obstruction in man led to the experimental work of McMaster, Broun and Rous<sup>9</sup> on the character of the bile secreted after relief of obstruction in dogs. Their method was to insert a drainage tube into the common duct and keep it

8 Judd, E. S., and Lyons, J. H. White Bile in the Common Duct, *Ann Surg* **77** 281, 1923.

9 McMaster, Philip D., Broun, G. O., and Rous, Peyton. Studies on the Total Bile. I. The Effects of Operation, Exercise, Hot Weather, Relief of Obstruction, Intercurrent Disease, and Other Normal and Pathologic Influences. *J. Exper. Med.* **37** 395, 1923. III. On the Bile Changes Caused by a Pressure Obstacle to Secretion and on Hydrohepatosis, *ibid.* **37** 685, 1923.

tively avirulent. As a result of the second operation all the clinical and bacteriologic signs of severe infection were noted. On the other hand, the control dog, which was killed four and one-half months after ligation and on which no second operation had been performed, had dark green bile and showed no signs of infection. There was an uneventful postoperative course, and bile obtained post mortem contained only *Staph. albus* and a few leukocytes. Dog 768 had a serious course following ligation of the common duct, while culture of the aspirated bile showed *Str. haemolyticus*. The other two members of group 2, however, from which green bile was obtained, showed no clinical symptoms until after the second operation. A consideration of these results leads me to the following conclusion:

Experimentation on dogs shows that white bile is produced in those cases of obstruction of the common duct in which infection is present and extends over a long period.

#### EXPERIMENTAL AND CLINICAL SIGNIFICANCE OF BACTERIA AND LEUKOCYTES IN THE BILE

In my experiments white bile yielded *B. coli* in two cases and *Str. haemolyticus* and *B. Welchii* in two others. With regard to the clinical cases, which will be reported later, the only sample of bile that was examined bacteriologically contained *B. coli* and *B. Welchii*. To evaluate properly the significance of the bacteriologic findings, one must refer to the literature on this subject. Bernhard reported the culture of *B. coli* in one case, staphylococcus in another and streptococcus in a third, while Melchior obtained *B. coli* once. On the other hand, Klose and Wachsmuth as well as Gorke<sup>22</sup> and Kausch obtained negative results in three cases in which white bile was found. On the basis of these findings Kausch not only denied the truth of the infection theory but went so far as to say that white bile can be produced only in the absence of infection.

A possible explanation for the negative bacteriologic findings reported in the literature may be that the bacteria at the time of examination were dead. To substantiate this idea, one has only to bear in mind the sequence of events which sometimes occurs in the case of a long-lasting abscess. The abscess in its acute stages may be swarming with micro-organisms, yet may become sterile and free from leukocytes after some time. Many cases illustrating this point have been reported in the literature. Josa<sup>23</sup> stated that the bacteria in an appen-

<sup>22</sup> Gorke, H. *Deutsche med. Wchnschr.* 48:1166, 1922.

<sup>23</sup> Josa, Ladislaus. Ueber einen seltenen Fall von Appendicitis phlegmonosa im obliterierten Wurmfortsatz. *Zentralbl. f. Chir.* 62:259, 1935.

clamped for twenty-four hours. The result was a copious secretion of bile with a low pigment content. In another series of similar experiments they produced a colorless fluid by putting a rubber bag into the abdominal cavity of the dog and connecting it with the common duct. The bag was emptied every twenty-four hours through an opening in the abdominal wall.

Further clinical information on relief of obstruction was added in 1930 by Walters and Greene,<sup>10</sup> who described four cases in which white bile was replaced by green bile after relief of an obstruction. These authors suggested that cholangitis may be of importance in the production of white bile.

The idea that infection may play a part in the production of white bile has been advanced by many authors. Among the first to give this thought serious consideration were Kummel and Gundermann.<sup>11</sup> Melchior<sup>12</sup> stressed the virulence of the bacteria as a factor in the production of colorless fluid in the ducts. In the Japanese literature Soejima<sup>13</sup> stated that infection is important in the genesis of white bile. Following this idea is the work of Bernhard,<sup>14</sup> who performed a great number of experiments on rats and rabbits and gave due emphasis to the problem of infection. He devised a method of keeping the animals alive long enough for the bile to finish its process of decolorization. By means of continuous injections of sucrose he prevented the death of the animals, which ordinarily occurred from insufficiency of the liver a short time after ligation of the common duct. In rats white bile was found from twenty-four to forty-four days after ligation. As a result of his first series of experiments Bernhard concluded that infection does not play an important rôle in the decolorization of bile. Further experimentation, however, led him to reverse his opinion. By ligation of the common duct in rats he obtained white bile in some instances and green bile in others. Observation showed that the rats from which the white bile was obtained had been afflicted with severe enteritis previous to the operation, while the others were normally healthy animals. On the basis of this observation he stated as his conclusion that infection may play some part, the bacteria traveling

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10 Walters, W., Greene, C. H., and Frederickson, C. H. The Composition of the Bile Following the Relief of Biliary Obstruction, *Ann Surg* **91** 686, 1930.

11 Gundermann, W. *Mitt u d Grenzgeb d Med u Chir* **39** 353, 1926.

12 Melchior, E. *Zentralbl f Chir* **58** 135, 1931, *Beitr z klin Chir* **139** 162, 1927.

13 Soejima, R. Ueber die weisse Galle und den Hydrops der gesamten Gallenwege, mit besonderer Berücksichtigung ihrer Aetiologie, *Zentralbl f Chir* **31** 1738, 1925.

14 Bernhard, F. *Deutsche Ztschr f Chir* **222** 66, 1930, *Zentralbl f Chir* **57** 194, 1930, *Beitr z klin Chir* **150** 82, 1930, **154** 389, 1932.



dix which has become stenosed as a result of inflammation lose their virulence and for the most part die

By analogy it is not surprising to find that old white bile is sterile. In my own experiments the bacteriologic examinations gave positive results in all cases even after four and one-half or five and one-half months. Perhaps the mildly virulent nature of the bacteria did not allow the process to complete itself within so short a time. In the only clinical case in which a bacteriologic examination was made the results were positive.

While negative bacteriologic findings do not necessarily speak against the infection theory, positive results form a strong support for it. It must be borne in mind in this connection that the gallbladder, according to the work by Andrews, has a normal bacteriologic flora, consisting of streptococci members of the *B. coli* group and *B. Welchii*. It is evident that no definite conclusions on this subject can be drawn from the bacteriologic findings alone.

Further valuable information about the presence of infection in cases in which white bile is found is given by the leukocyte content, which is greatly increased in the presence of infection.

White bile, in clinical reports, is often referred to as milky bile and is described as a white flaky material mixed with colorless fluid. The French refer to this as *bile laiteuse*, while in the protocols of one of my own clinical cases the colorless fluid is described as milky. Unfortunately, not many microscopic examinations of this material have been made. It is possible that white bile consists, in part at least, of cholesterol. Nevertheless the microscopic diagnoses that have been made indicate that these flakes consist in large part of leukocytes as well. The rôle played by the leukocytes in effecting this decolorization is best illustrated in the extreme but rare condition of purulent cholangitis in which the green hepatic bile is replaced by a colorless purulent fluid. Probably the most purulent stage had already been passed at the time of examination, thus accounting for the small number of bacteria and leukocytes found.

Thus, in evaluating the pathogenesis of white bile one may say with some assurance that bacteria and leukocytes, if not present at the time of examination, were present at least at some time during the development of the colorless fluid.

There are two possible routes by which bacteria may enter the bile. One is by direct ascension up the ducts as in infection due to the presence of a calculus, the other is a hematogenous spread from the intestine by way of the portal vein into the biliary system.

through the intestinal wall and by way of the portal vein into the stagnant bile. Further experimentation on rats in which intestinal infection was produced by means of a special diet of milk or such drugs as sodium bicarbonate or castor oil seemed to verify this idea.

My own work<sup>15</sup> in relation to this problem showed further the importance of infection of the stagnant bile. In my experiments I used rabbits, which by special treatment can be kept alive long enough. The biliary system of this animal is especially sensitive, and changes in the bile occur rapidly.

Briefly, the results of my experiments were as follows. Ligation of the common duct in seventeen rabbits was followed by the production of white bile in four instances. In those four cases only one sample of bile was found to be sterile, the others containing *Bacillus coli* and streptococci. Seven days after ligation was the shortest time in which white bile occurred. The liver showed little cholangitic reaction. A striking fact was that in cases in which white bile was collected the hepatic cells showed relatively little changes, whereas in cases in which green bile was found the liver showed extensive necrosis and cirrhosis and contained almost no functioning parenchyma.

As regards infection I could formulate only a reserved opinion, as my observations were based only on the bacteriologic and leukocytic content of the white bile. Moreover, the bacteriologic results were not certain, since the animals died spontaneously and the bile could be examined only at a later date, leaving open the possibility of a post-mortem invasion by bacteria. I concluded from my experiments that infection may play a role in the pathogenesis of white bile in rabbits and that, in addition, the condition of the hepatic cells may play some part, since I found a correlation between white bile and a well functioning liver, on the one hand, and green bile with an extremely damaged liver, on the other.

This brief review of the literature shows that the problem of white bile is not yet solved. The mechanical theory of Quincke and Kausch was soon replaced by the idea of a functional secretory process. The white and green systems of Rous and McMaster, however, could apply only to experiments on animals in which no infection occurred. The authors themselves stated that they focused their attention mainly on the cases in which there was no infection. Rous in one of his discussions stated:

In a dog from which we were making day to day collections of the bile from different portions of the liver infection occurred in one of the duct systems drained by rubber tubes. Almost at once its output became thickly mucinous and prac-

15 Aronsohn H. G. Weiße Galle im Tierexperiment und in der Chirurgie, Beitr. z. klin. Chir. **156** 63, 1932.

## CLINICAL CASES

Few clinical cases in which white bile was found have been reported in the literature. It may be of some value to report a few such cases in this regard and to study the pathogenesis of white bile on the basis of the clinical cases available.

Examination of the records of operation on the common bile duct at the University of Chicago Clinics for the last five years reveals that there was only one outspoken case of white bile. There were three other cases in which the bile either was light green or on chemical examination showed so little of the normal bile constituents that I feel justified in considering them in this discussion.

It would be well to mention at this point that my observations were not made on bile collected from the liver in all the cases to be reported. Nevertheless, since drainage of the gallbladder resulted in a collapse of the dilated bile ducts, I feel justified in assuming that the bile aspirated from the gallbladder represented that present throughout the entire liver-gallbladder system.

The obstruction was caused in one case by carcinoma of the head of the pancreas and in another by a stone in the common duct. In two other cases it resulted from old injuries following operations for stones in the common duct.

The prognosis on the basis of these cases is favorable. In view of the fact that one patient died of peritonitis ten days after the operation, the mortality, as far as I can judge from the few cases cited, corresponds fairly well with Judd's figure of 21 per cent.

CASE 1—Mrs. E. A., aged 35, had a history of pain in the epigastrium and the right upper quadrant of the abdomen beginning twelve years previously. She did not remember whether she had been jaundiced. Seven years before admission the gallbladder, which she said contained stones, was removed, and since that time the patient had had periods of jaundice, chills, tenderness in the epigastric region and itching. Attacks occurred with great irregularity, sometimes lasting for ten days. The present attack had lasted for one week and had consisted of tenderness in the epigastric region, chills, nausea, vomiting, jaundice, itching and a temperature as high as 102 F.

At operation a short bile duct was found anastomosed to the duodenum or stomach in a mass of adhesions. No stones were palpable. It seemed probable that there had been an injury and possible resection of part of the common bile duct followed by anastomosis of the duodenum and the hepatic duct. The bile duct was seen to contain a clear white fluid. Nothing was done at the operation except free the ducts from adhesions. The postoperative course was normal and satisfactory.

This case clearly illustrates the clinical picture seen in cases in which white bile is found. The clinical history revealed that attacks of pain in the right upper quadrant had occurred irregularly for seven years.

tically lost its biliary character, being but faintly tinted with bilirubin, whereas the companion bile that served as a control was thin and dark

These authors considered the occurrence of an infection a complication which made their results unpredictable "Infection may so change the gall bladder that a white system develops, where a green one is expected"

It is possible that this infection, observed incidentally by Rous and considered an unnecessary complication in his experiments, is actually a vital factor in the pathogenesis of white bile

Further proof of the dubiousness of Rous' theory is given by the experiments of Bernhard on rats. Since the rat does not have a gall-bladder, ligation of the common duct naturally results in the appearance of the white system of Rous and leads one to expect the production of white bile in all such cases. Nevertheless, in thirty such animals Bernhard found white bile only once.

Another fact supporting the idea that infection is the probable cause is that obstruction of the common duct which results in the production of white bile in man is caused most often by a stone which is accompanied by infection more frequently than is any other cause of obstruction.

One of the chief obstacles in the study of this problem has been the lack of bacteriologic examinations of the white bile.

Aschoff<sup>16</sup> and Gundermann have shown that colorless hydrops of the gallbladder is often produced by infection. One cannot, however, draw a parallel between white bile and colorless hydrops of the gallbladder. In the first place, the function of the mucous membranes of the ducts and that of the mucous membrane of the gallbladder are very different, as Rous has shown. The obstructed gallbladder, moreover, is a system in which only the mucous membrane of the gallbladder can influence the bile, whereas when the bile ducts are obstructed not only the mucous membrane of the ducts but also the hepatic cells may play an important part.

For these reasons one cannot properly draw an analysis between the pathogenesis of white bile and that of colorless hydrops of the gallbladder. Bernhard, as previously mentioned, artificially produced intestinal infection in rats and obtained white bile after ligation of the common duct. This indirect method of producing infection of the biliary system, however, cannot be considered a final proof of the correctness of the theory of infection. My method was to produce infection of stagnant bile in dogs directly by injection of bacteria into the obstructed biliary system.

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<sup>16</sup> Aschoff, L., and Bacmeister, A. *Die Cholelithiasis*, Jena, Gustav Fischer, 1909.

after cholecystectomy for cholelithiasis. These attacks, lasting as long as ten days, had been accompanied by more or less severe jaundice, fever, chills and tenderness.

In this case there were short recurrent attacks, due to more or less complete obstruction, which disappeared in a few days without treatment. Fever, chills and epigastric tenderness pointed toward an inflammatory process in the biliary system, but the exact nature of this process is not known. It may have been either secondary cholangitis following primary mechanical obstruction or primary cholangitis causing obstruction by swelling of the mucous membrane. Which of these processes had taken place is of no consequence for this discussion. The significant point is that the common duct was obstructed at intervals over a long period, with accompanying infection.

On the basis of these facts it was no surprise on operation to find colorless bile. In fact, the shortness of the duration of the attacks as well as the mild nature of the jaundice and infection led me to expect a less completely decolorized bile. The findings at operation explained this discrepancy, since obstruction was found to be more complete anatomically than the clinical symptoms indicated.

CASE 2—Mrs. I. M., aged 35, for the past four years had had an intermittent dull pain in the right lower quadrant, without any fever, tenderness, nausea, vomiting or jaundice. A roentgenogram revealed stones in the gallbladder.

On Oct. 18, 1929, cholecystectomy was performed. The gallbladder contained numerous greenish stones, but there were no signs of acute infection. A few days later, however, as a result of injury during the operation, the common duct was completely obstructed.

On October 29 the common duct was repaired and a T tube inserted. The postoperative course was uneventful. The biliary discharge was profuse at first. During the next two years, however, the patient had frequent attacks of pain, fever and jaundice.

In January 1931, because of severe pain, profuse diarrhea, jaundice and pruritus, a diagnosis of cholangitis and obstructive jaundice was made.

On March 19, 1931, the common duct was again repaired and a T tube inserted. Daily specimens of bile were obtained until the tube was withdrawn forty days after operation. For a few days after the operation the flow from the tube was scanty, and the material was light, as one would expect after relief of obstructive jaundice. From then until the tube was withdrawn, however, the bile was of normal appearance. Chemical examination by the aminonitrogen method showed absence of bile salts and an unusually low cholesterol content for nearly three weeks. The values soon rose to fairly normal levels, however.

This case is very similar to the preceding one. Cholecystectomy resulted in such severe injury to the common bile duct that a few days after operation there was complete obstruction, making necessary a second operation. A T tube was inserted, and a profuse bilious discharge appeared. This fistula remained in place for two years, and during that period the patient had frequent attacks of pain in the upper

## EXPERIMENTATION ON ANIMALS

The procedure was as follows. Ligation of the common duct was performed, accompanied in a few cases by a cholecystectomy, to determine whether the biliary system would react differently without a gallbladder. This was followed four weeks later by a second operation, at which bile was aspirated and bacteria were injected into the walls or cavities of the gallbladder and bile ducts. Infection occurred either spontaneously after ligation of the duct or after injection of bacteria. Cultures were made of the aspirated bile. The dogs either died spontaneously or were killed after from four and one-half to five and one-half months. The animals were constantly observed for any signs of infection, special emphasis being placed on the bacteriologic examination of the bile at different stages.

I chose the dog for my experiments, since this animal survives for many months after ligation of the common duct, thus permitting observations to be made for a much longer period than is possible with rabbits and rats. Moreover, a second operation can be performed on dogs with much less risk than on smaller animals.

The operations were performed with the animals under ether anesthesia and with strictly aseptic conditions. Obstruction was produced by double ligation of the common duct and transection between the two ligatures.

In every case great care was taken to determine the presence or absence of an accessory duct. In no instance were the ducts found to be grown together at any time after the operation. The wounds for the most part healed well, with the exception of a few small stitch abscesses.

Various strains of bacteria were used for the injections, *Bacillus coli* yielding the best results. *Staphylococcus aureus* and *Staphylococcus albus* did not produce the desired infection in all cases, while some highly virulent organisms, such as *Streptococcus haemolyticus*, were fatal to the animal in a short time.

A suspension of the bacteria in saline solution containing about a billion organisms per cubic centimeter was used. Two cubic centimeters of this suspension was injected into the walls and cavities of the bile ducts and gallbladder.

I used the following features as criteria of the presence of infection in my clinical observations: degree of apathy, ability to take nourishment, quality of the stool and the presence and extent of jaundice.

Different parts of the gallbladder and bile ducts were selected for the aspiration whenever possible. A bacteriologic examination of the bile was made in every case, and also a chemical analysis and a sediment test whenever there was sufficient material. The bilirubin content was determined by the method of Schmidt and Jones,<sup>17</sup> the cholesterol content by that of Bloor<sup>18</sup> and the content of bile acids by that of Schmidt and Dart.<sup>19</sup> Histologic examinations were made in every case.

Ligation of the common duct was performed on eleven dogs, with superimposed cholecystectomy in two cases. Four of these dogs, constituting group 1, died from two to twenty days after the first operation. Six of the seven remaining

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17 With reference to the bilirubin determinations, it should be stated that there are no strictly accurate methods, but I have used the method of Schmidt and Jones, which I believe to be the most accurate method in use at present (Schmidt C. R., and Jones, K. K. A Method for the Determination of the Total Pigment in Bile, *Proc. Soc. Exper. Biol. & Med.* **34** 17, 1936).

18 Bloor, W. R. The Determination of Cholesterol in Blood, *J. Biol. Chem.* **24** 227, 1916.

19 Schmidt, L. W., and Dart, A. E. Estimations of Bile Acids in the Bile, *J. Biol. Chem.* **45** 145, 1920.

part of the abdomen, jaundice of varying intensity and fever. During those attacks the flow of bile from the fistula ceased. The stool was clay-colored and the urine dark. The clinical diagnosis was obstructive jaundice and cholangitis. The last attack, of special severity, lasted for seven weeks and was accompanied with profuse diarrhea, making necessary another operation and the insertion of a T tube. For a few days after the operation the bile issuing from the tube was light-colored, and then it became normal again.

This was a case of biliary stasis accompanied with infection. The individual attacks were of short duration, indicating that the inflammatory process was mild. However, the last attack, which led to operation, was of special severity and of long duration (seven weeks) and was characterized not only by cholangitis but by profuse diarrhea. It is highly probable that the last obstruction was chiefly responsible for the change in the character of the bile. The bile would probably have been completely discolored if the previous attacks during the last two years had been the result of complete obstruction.

CASE 3—Mr. I. D., aged 73, for the past four years had had attacks of pain in the right upper quadrant of the abdomen, radiating to the right shoulder. Two of the attacks were especially severe and were accompanied with nausea and vomiting, followed by jaundice, which lasted for six weeks. The attacks were all accompanied with chills, fever and tenderness in the right upper quadrant. The last attack was especially severe, occurring from ten to fourteen days before admission and accompanied with pain similar to that previously mentioned, chills, fever and the excretion of dark red urine.

On admission to the hospital the patient had jaundice and pain. At operation a stone was removed from the common duct, and a T tube was inserted. There were adhesions to the gallbladder, which was slightly thickened. The common duct was greatly dilated. There were about twenty-five stones in its lower portion and about thirty-five in its upper portion and in the hepatic ducts.

Daily drainage yielded on the average from 300 to 400 cc. of fairly clear bile. Chemically the specimens for the first four days contained a small amount of cholesterol, but the amount rapidly became normal. Not one of the daily specimens contained any bile salts.

The patient died of biliary peritonitis on the tenth day. At autopsy both the hepatic and the common duct were increased in diameter, and five stones were present in the latter. The liver weighed 1,550 Gm., and the cut surface was somewhat opaque and brownish rather than green. Microscopically there was a considerable increase in the amount of periportal connective tissue, and in some places there was marked round cell infiltration. A diagnosis of beginning biliary cirrhosis was made. Bacteriologic examination of the bile showed *B. coli* and *B. Welchii*.

In this case there was a history of severe attacks due to the presence of gallstones for the last four years, two of the attacks being especially severe and indicating the presence of complete obstruction. These attacks were accompanied with vomiting, nausea, fever and chills and were followed by jaundice, lasting as long as six weeks. Operation

animals were subjected four weeks later to a second operation, which consisted of aspiration of bile from the gallbladder and injection of bacteria. The seventh animal was used as a control. Group 2 consisted of three dogs which died from one to thirteen days after the second operation. The three other dogs and the control dog, which remained alive and were killed from four and one-half to five and one-half months later, constituted group 3. This last group included the two dogs on which cholecystectomy was performed.

There follow three protocols of dogs in which the character of the bile showed a significant change and the protocol of the control animal. The bile from all the dogs in group 1 and from two members of group 2 was grossly normal with respect to coloration, hence the protocols for those dogs have been omitted. The bacteriologic results for all the specimens, however, are of significance and have been included in table 1.

Dog 415—The first operation, consisting of ligation of the common duct and cholecystectomy, was performed on June 19. Severe jaundice developed, and the stool was colorless. There were no marked symptoms. The animal recovered in a short time. Persistence of a small stitch abscess was noted.

The second operation was performed on July 17. Extensive adhesions were present, and the common and the hepatic duct were markedly dilated. Aspiration yielded a small amount of dark green bile. Two cubic centimeters of a suspension of *Staph aureus* in saline solution was injected into the wall and the cavity of the common duct. A bacterial culture gave negative results. A few leukocytes were observed in the sediment.

The postoperative course was severe, the animal was completely apathetic for twelve days and refused to take food. Signs of recovery were noted after three weeks.

On December 5 the dog was electrocuted. Postmortem examination showed an abscess of the spleen as large as a kernel of rice. Extensive adhesions were noted around the common duct, which was 1 cm in diameter. The diameter of the cystic duct measured 6 mm. The intestinal mucosa was red and hyperemic. Three cubic centimeters of mucinous, watery, clear fluid was aspirated.

Culture of the bile yielded *Str haemolyticus* and *Bacillus Welchii*. Chemical analysis showed that no bilirubin, cholesterol or bile acids were present. The sediment contained many leukocytes.

In the liver there was marked fatty infiltration, some areas being spared. No pigment was present in the hepatic cells, but a good deal was present in the capillaries. Little interstitial round cell infiltration was seen.

Dog 772—The first operation, consisting of ligation of the common duct and cholecystectomy, was performed on July 25. Severe jaundice developed, and the stool was colorless. There were no marked symptoms. The animal recovered in five days.

The second operation was performed on August 23. Extensive adhesions were present between the duodenum and the liver. The common duct was in the depth of these adhesions and not greatly dilated. The hepatic duct was only slightly dilated.

Aspiration yielded 0.5 cc of dark green bile. Two cubic centimeters of a suspension of *B coli* in saline solution was injected into the wall and cavity of the common duct. Bacterial culture yielded *Staph albus*.



revealed a greatly dilated common duct obstructed by stones. A T tube was inserted and the bile collected. The bile was clear and on chemical examination showed an absence of bile salts and a low concentration of cholesterol. After four days, however, the bile became normal. At postmortem examination the bile was seen to contain *B. coli* and *B. Welchii*. Grossly the liver was abnormally light green, while microscopically there were areas of round cell infiltration and a tendency toward biliary cirrhosis.

The clinical history as well as the postmortem examination showed all the necessary conditions for the pathogenesis of white bile. There was complete obstruction of the common bile duct, accompanied with an infection of the liver that was so severe as to cause the appearance of beginning biliary cirrhosis. White bile was obtained, as would be expected, but it was not as completely decolorized as the conditions present indicated that it would be. It is possible that the presence of a gallbladder that was fairly normal anatomically operated against the formation of white bile by favoring concentration.

CASE 4—Mr. O. H., aged 69, had been jaundiced, without remissions, for six months, and at the same time severe diarrhea had developed. The stools were colorless, but the diarrhea disappeared after the patient was placed on a special diet, only to reappear two weeks before his admission to the hospital. The patient had lost 50 pounds (22.7 Kg.) in the last year and for the past six weeks had had abdominal distention and edema of the legs. At no time did he have pain. The temperature before operation was 100.5 F.

Operation revealed the presence of carcinoma of the head of the pancreas. The common duct was greatly dilated (3 cm. in diameter) and tense. The gallbladder was greatly distended and contained about 100 cc. of turbid brownish, milky bile. When this material was aspirated from the gallbladder the common duct collapsed. Exploration revealed a patent cystic duct and carcinomatous metastases in the liver. Cholecystogastrostomy was performed, and four days later bile was found in the stool. The patient left the hospital in good condition.

The history of this patient is of particular interest in that biliary stasis was accompanied with intestinal infection. The stasis was caused by a carcinoma of the head of the pancreas, which was responsible also for the complete obstruction of the common duct and the jaundice of six months' duration. The condition was accompanied with severe diarrhea, although there were no symptoms of infection of the biliary system. The extreme dilatation of the bile ducts and gallbladder observed at operation was an anatomical indication of the completeness of the obstruction. The bile that was aspirated from the gallbladder was partially discolored. One may safely assume that the bile from the liver was of the same nature, since puncture of the gallbladder resulted in collapse of the duct system.

The occurrence of intestinal infection with obstruction of the common duct and biliary stasis corresponded to the results obtained by

crystals dissolved in spinal fluid cause so much headache. Such a solution is strongly hypertonic and to that degree is irritating. In the cat at least the matter of isotonicity is of great importance. In that animal the exposed cervical cord can be edematized with Ringer's solution with no disturbance at all, but if the Ringer's solution is diluted with distilled water the cat dies within a few seconds. Finally, the temperature of the injected solution is important. There is no question that the injection of a cold solution into the subarachnoid space is irritating and harmful.<sup>3</sup>

Besides these positive characteristics of injected fluids it is to be remembered that solutions brought into prolonged contact with the tissues of the central nervous system may be irritating because of what they lack. The most common clinical demonstration of this is the violent headache which follows the introduction of air into the cerebrospinal space in ventriculography.<sup>4</sup> As it is saturated almost immediately by water vapor, it is impossible to think of the air as an irritant per se, but by virtue of what it keeps away from the tissues, in practical results it is an exceedingly severe irritant. Weed,<sup>3</sup> studying the reactions of the meninges in cats, found that the lack of calcium has a similar result. Any solution which lacks a trace of that element is irritating and will cause the death of the animal in a few hours.

The first step of the present investigation was the development of an anesthetic solution as nearly as possible free from irritating properties. Procaine hydrochloride is the least irritating of suitable drugs. A solution of procaine hydrochloride of a concentration of 5.48 per cent is isotonic. I have used various combinations of procaine hydrochloride with dextrose and saccharose in order to increase the viscosity of the solution, but so far as my experience goes a simple solution of procaine hydrochloride of a strength from 5 to 5.5 per cent is just as good as any of the combinations. To such a solution calcium chloride is added in a quantity sufficient to make its strength 0.024 per cent, this figure being taken from Weed's work on cats. In the winter this solution is warmed to body temperature before injection. In the summer Muscat is so warm that this point requires no attention. The  $p_H$  of the solution is set between 7 and 7.2.<sup>5</sup>

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<sup>3</sup> Weed, L. H., and Wegeforth, P. *J. Pharmacol. & Exper. Therap.* **13** 317, 1919.

<sup>4</sup> Sachs, Ernest. *The Diagnosis and Treatment of Brain Tumors*, St. Louis, C. V. Mosby Company, 1931, pp. 342 and 123.

<sup>5</sup> Dr. W. C. Harden of Baltimore worked out the details of this solution. It was the hope originally that we could work together on a much more thorough investigation of the problems of spinal anesthesia, the chemical problems as well as the clinical ones, but Muscat and Baltimore are too far apart for that to be practicable.

The limitations of such a solution are obvious. It will afford an anesthesia of an hour to an hour and a quarter but not more. It is a heavy solution, as indeed any effective solution of procaine hydrochloride must be unless diluted with something like alcohol. Therefore it cannot be used with the patient in the Trendelenburg position and is unsuitable for operations in the upper portion of the abdomen, when it is imperative that the patient be in the Trendelenburg position to maintain the blood supply to the brain and usually for the actual operative procedure as well. In Muscat nupercaine is used for such operations.

With the introduction of this nonirritating solution severe post-anesthetic headache has disappeared, and the postoperative comfort of the patients is gratifying. The clinical impression is that when this solution can be used the problem of spinal headache has been disposed of.

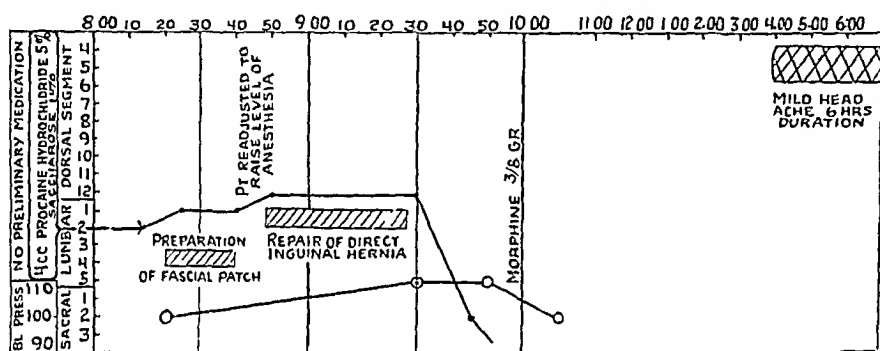


Fig 1—A clinical picture confused by morphine given postoperatively to a high-strung Persian aged 32. The headache occurred six hours after the disappearance of the anesthesia and continued until the patient went to sleep at 10:00 p.m. Headache was not present on the following morning. The systolic blood pressure is indicated by the circles. The height of the anesthesia in segments is indicated by the solid dots. The arrow shows the level at which the anesthetic was introduced and the time of its introduction. The shaded areas indicate the operations, and the cross-hatched area, the headache.

Unfortunately this impression is not entirely correct. Questioning shows that many patients suffer from headache which is too mild to cause complaint. Moreover, they are comfortable only if they remain recumbent. Those who sit up and walk around after the operation frequently suffer from headache, which may be very severe and persistent. This was a disappointment, for in Arabia operations must be performed on many patients who wish to walk home afterward, and no method of anesthesia can be regarded as satisfactory unless it makes this possible.

The study of this form of headache offers certain difficulties. Postoperative medication can mask such a headache. Figure 1 is the chart for such a case. Various causes may result in headache quite uncon-

Bernhard in his experiments on rats. The carcinoma of the head of the pancreas probably was instrumental in the production of diarrhea by way of the pancreatic enzymes. This then resulted in an intestinal infection, which may have caused secondary involvement of the biliary tract and thus probably explains the sequence of events.

In addition to the cases just discussed in which white bile was found, I shall describe two cases in which long-lasting stasis of the bile did not result in decolorization. To illustrate this condition, I have chosen two cases of congenital obstruction, since it is easy in these cases to demonstrate why the bile does not undergo any change.

CASE 5—R. C., aged 1 month, was seen to have blue spots on the face immediately after birth but was otherwise normal. On his admission to the hospital, four weeks after birth the infant's skin was very dark, the scleras were yellow and the mucous membrane was pigmented. The liver extended 2 fingerbreadths below the costal margin, the urine was dark green and contained bilirubin and the stool was clay-colored. Operation revealed complete obliteration of the common and the hepatic duct. The liver was greatly enlarged and slate black. The gallbladder was thin and somewhat distended and contained clear golden yellow bile. An anastomosis was made between the fundus and the anterior wall of the stomach. Culture of the bile showed no growth. There was no fever, and the postoperative course was excellent.

Immediately after birth there were signs of complete obstruction of the common duct, i. e., clay-colored stool, general severe jaundice, urine containing dark green bile and hemorrhages in the skin of the face. The general condition of the patient, however, was little disturbed, there being no pain or fever, and the intake of food was normal.

Operation, performed thirty days after birth, revealed normally colored bile in the gallbladder and a strikingly dark liver, apparently rich in bile pigments. The finding of green bile in a case of congenital obliteration of the bile ducts of thirty days' duration is not at all surprising. Neither clinically nor anatomically were there any signs of infection accompanying this stasis. This was further substantiated by the sterile bacteriologic cultures.

Since white bile has been seen to be produced after a period of obstruction lasting for sixteen days, an obstruction of thirty days' duration would surely be long enough for white bile to be produced. Besides, this stasis may have been of still longer duration than thirty days, since obliteration of the ducts may have occurred during fetal life.

CASE 6—I. D., aged 5 months, had become increasingly jaundiced since two days after birth. He had gained weight poorly, the stools had always been white and the urine was deep orange. On admission the infant was intensely icteric, not well developed and poorly nourished but did not appear acutely ill. The liver was greatly enlarged, the urine contained bilirubin and examination of the stool revealed no urobilin.

With the animal under light ether anesthesia the common duct was tightly ligated and then divided within a half-inch of its entrance into the duodenum. In four of the control dogs and in one of the others the gallbladder was removed at the same time.

At intervals of from four to thirty-six days after the original operation the obstruction was released in six dogs, under the same type of anesthesia and through the same scar. Cholecystectomy or choledochostomy was done, according to whether or not the gallbladder had been removed. The dogs were then killed after various intervals, as the tables show. In the case of the single dog which died of natural causes after the second operation autopsy was performed within an hour after its death.

Clinically the result of the experimental obstruction was the same in all the animals. Jaundice developed in all, the degree depending on the duration of the obstruction, and all exhibited varying degrees of anorexia, listlessness and

TABLE 2—*Experimental Findings on Six Dogs in Which Decompression Was Done*

Dog	Procedure	Duration of Obstruction, Days	Duration of Decompression	Observations
10	Ligation and division of the common duct cholecystomy	4	3 $\frac{1}{2}$ days	Not significant
15	Ligation and division of the common duct cholecystectomy choledochostomy	7	2 $\frac{1}{2}$ hours	Not significant
12	Ligation and division of the common duct, cholecystomy	14	6 days	Not significant
6	Ligation and division of the common duct cholecystomy	14	7 days	Natural death immediate autopsy, multiple hepatic abscesses no change in the biliary ducts
13	Ligation and division of the common duct cholecystomy	20	4 days	Columnar type of epithelium in lining cells of small and medium sized ducts
5	Ligation and division of the common duct, cholecystomy	36	4 days	Columnar type of epithelium as in dog 13 marked fatty change in central area of lobules

loss of weight. The highest icteric index was 120, but further laboratory studies showed no other significant changes except the appearance of bile in the urine. At the second operation exploration revealed no free fluid in the abdominal cavity or any other evidence of infection. Whenever the gallbladder was still present, it was markedly distended, as was the whole extrahepatic biliary tree. The tension in the bile ducts, particularly in the common bile duct, was naturally much greater when the gallbladder was not in situ. The bile in all instances was thick and black. The degree of jaundice in the tissues varied with the duration of the obstruction, as did the size and color of the liver, which was always enlarged and dark green.

The immediate flow of bile through the catheter inserted into the gallbladder or the common bile duct and the continued drainage of bile through it until death made it clear that the obstruction had been completely released. In two animals the tube was clamped off at intervals and was later released but this variation of the usual procedure produced no significant change in the chemical composition of the blood or in the urine.

At operation the liver was observed to be hard and somewhat enlarged, and the gallbladder was very small, containing 2 cc of clear mucus. An attempt was made to find the hepatic duct by means of an aspirating needle, but without success. The gallbladder was opened, and its cavity was packed with gauze which was then led to the surface. The infant died one day later of bronchopneumonia.

At autopsy the liver was observed to be hard and green. All lobular markings were obliterated by a diffuse infiltration of whitish tissue. The gallbladder contained no bile, and its mucosa was not bile stained. The cystic duct, common duct and ampulla of Vater were not patent, and the hepatic duct was absent. On section the liver showed a marked growth of fibrous connective tissue in the portal triads but only a few polymorphonuclears and lymphocytes. In this connective tissue and about the periphery of the lobules there was a marked increase in the number of bile ducts, the ducts often containing dark masses of bile pigment. The capsule of the liver was greatly thickened and contained many bile ducts. Many of the capillaries were distended with bile, especially those in the center of a lobule.

This case is very similar to the preceding one except that at operation thick green bile was found only in the liver, while the gallbladder contained clear mucus.

The clinical picture revealed no signs of infection. While it is true that the infant was poorly developed and poorly nourished, it is specifically stated in the history that he was not acutely ill. The absence of infection, proved anatomically as well as clinically, could account for the finding of thick green bile in the liver. But how can the presence of clear fluid in the gallbladder be explained? If the contents of the gallbladder had originally been green bile, there is no reason to believe that it alone, and not the bile from the liver, should have become discolored. This is readily understood if it is assumed that the hepatic ducts were already obliterated when the liver became functional during fetal life. That would have prevented the gallbladder from ever receiving any bile. The slight amount of mucus present had probably been secreted by the mucous membrane of the gallbladder itself, stimulated by the stasis.

#### PATHOGENESIS OF WHITE BILE

*Closed System*—On the basis of the foregoing evidence one can now offer a likely explanation for the fact that in some cases of obstruction white bile is obtained and in others green bile. White bile is probably produced by an infection of stagnant bile which has existed for a long time.

This point is one of the most important factors in the understanding of the pathogenesis of white bile. One must next attempt to determine the function of infection in the process and, in addition, to explain what white bile is. Does infection have the power to change green into white bile, or is white bile the product of infected bile ducts, after the green bile has been in some manner removed?

The animals in which simple obstruction had been done were killed in from four to thirty-six days, the animals in which subsequent decompression was done were killed in from two and one-half hours to seven days. In no instance was there any evidence of peritonitis, and the observations at autopsy on the control group paralleled the observations on the other group at the second operation, when decompression had been done. In all the dogs in which decompression had been done the liver had decreased in size and the jaundice had decreased in degree. The only notable gross changes were in dog 6, in which the liver was studded with small abscesses seven days after decompression, and in dog 13, in which the liver was peculiarly soft and friable four days after decompression.

Histologic study of sections of the livers of both groups of dogs showed various degrees of necrotic change in the liver cells, especially those in the inner third of the lobule and about the large bile ducts. In no instance, however, did it approach the degree of necrosis noted in either the clinical or the experimental cases of "liver death" studied in our first report. The less marked character of the necrotic change is easily explained. The dogs in which obstruction was continued longest in this group of experiments did not have their gallbladders removed, as did the dogs in which necrotic changes were observed in our first series of experiments.

These necrotic changes are purely mechanical and are the direct result of the increase in the intrahepatic pressure which follows experimental obstruction of the bile duct. When the gallbladder is in situ, it serves as a sort of buffer, in that it absorbs and concentrates the bile, thus reducing it in quantity, and it acts also as a reservoir for bile. As a consequence, the rise in intraductal pressure, as well as the subsequent rise in intrahepatic pressure, is more gradual than is the rise in pressure when the gallbladder has been removed. When cholecystectomy has been done in addition, the intrahepatic ducts and the intraductal hepatic system in turn become enormously dilated as bile accumulates and biliary stasis increases. The pressure in the intrahepatic vascular tree must rise correspondingly to permit the liver cells to function at all, and it is a physical phenomenon that the cells first become atrophied and then, as the pressure increases, exhibit all gradations of change from simple degeneration to actual necrosis. That, if we may so express it, is the normal pathologic picture that follows biliary stasis.

When the biliary obstruction is released, on the other hand, and particularly when it is abruptly released, the first consequence is a reactionary hyperemia. The second consequence is a still more marked necrosis of the liver cells, from which, as the blood supply in them increases, the products of the necrotic change are swept out into the circulation, just as we have postulated in the theory we have advanced.

Since such changes take place in the liver cells, it might be assumed that similar changes would take place in the bile ducts and that their lining cells would show, first of all, some degree of flattening. In only

Concerning the mechanism of decolorization, I again refer to the studies of Gundermann and Bernhard. The former showed in his studies on hydrops of the gallbladder that decolorization is brought about by the action of leukocytes, which take up the bile pigment and digest it by means of their ferments. Bernhard in his studies on rats, observed the same phenomena in hepatic bile. In my experimental work I was unable to find bile pigment in leukocytes, and I attribute this to the fact that the process was more or less completed after four and one-half or five and one-half months.

On the basis of these studies I feel certain that the mechanism of decolorization is brought about by the action of leukocytes on the bile pigment.

To understand properly the pathogenesis of white bile one must first know the normal physiologic mechanisms at work in the gallbladder and bile ducts. The studies of Kausch and his successors are significant in this regard. According to these authors bile is a mixture of secretions from the liver and the bile ducts. If the secretion from the liver should suddenly stop, one would expect to find the bile ducts filled with a colorless fluid which without any doubt, would be a secretion of the ducts. Unfortunately, this cannot be proved in the experimental animal, because the hepatic secretion cannot be completely and suddenly cut off. Furthermore, even if this were possible, there would still remain a quantity of hepatic bile in the biliary system, and any fluid which was recovered would represent a mixture of the hepatic bile with the fluid produced by the ducts.

The methods used by Rous to prove the large quantity of fluid secreted by the ducts was double ligation of the ducts and aspiration of the secretion from the isolated portion. It seems doubtful to me, however, whether the enormous secretion obtained by Rous can really be considered as physiologic. It is easier to consider that the secretion was an abnormal one brought about by the double ligation which acted at least as a mechanical, if not an infectious, stimulus for secretion.

Another fact of fundamental importance in the understanding of the physiologic processes involved is the concentrating effect of the gallbladder. This was well shown by Rous and McMaster, who introduced hepatic bile into the empty gallbladder of the living dog and recovered it from twelve to twenty-four hours later. The bile which they recovered was found to be much more concentrated than the original bile. It is evident from this that if the gallbladder is cut off from the liver-bile system, either anatomically or functionally a less concentrated bile will be obtained.

Further data on the physiologic mechanisms involved can be obtained from the studies of Rous on white bile. I cannot concur with his con-



four of the experimental animals was any change noted in these cells but in all of them it was of this sort. In dog 16 in which the bile duct had been obstructed for eighteen days there was noted a slight degree of flattening of these cells. In dog 4 in which the bile duct had been obstructed for thirty-six days, more marked changes of the same sort were noted. In dog 5 in which the bile duct had been obstructed for thirty-six days and decompressed for four days and in dog 13 in which the bile duct had been obstructed for twenty days and decompressed for four days it was observed that the cells were of the columnar type which seemed to suggest that they had been flattened but that they were springing back to their normal state. All the changes were noted in the small and medium-sized ducts. The epithelium of the large ducts showed no change.

Histologic study of sections of the liver showed in all instances the usual reaction of round cell infiltration and of polymorphonuclear cells. These changes however are not peculiar to either biliary stasis or its release.

These negative histologic observations may be interpreted to indicate that the lining cells of the biliary tree play no part in the production of the liver-kidney syndrome. Indeed if our theory be correct that this syndrome is apparent in other pathologic states as well as in disease of the biliary tract it is scarcely reasonable to suppose that they could play any part since the ductal system of the biliary tract is not concerned in these other conditions. The absence of positive findings in the lining cells of the biliary ducts seems to us another link in the chain of evidence pointing to the liver cells as the source of the lethal toxin in the liver-kidney syndrome.

In view of our own negative results in these experiments it was at first rather disconcerting to find exactly reverse results reported by Stewart and Cantarow<sup>4</sup> in a somewhat similar series of experiments on nineteen cats. Experimental obstruction was continued in these animals for from one to sixteen days and was followed by decompression for from one hour to seven days. The principal changes which they noted were

1. A progressive proliferation of the cells of the mucosa and of the cells lining the biliary ducts followed obstruction and finally amounted to papillary and adenomatous changes.

2. Mitosis and budding of the cells in the smaller ducts were present as early as twenty-four hours after obstruction had been done. In the small and the medium-sized ducts the enlargement of the epithelial and infiltrating cells was at times so marked as to occlude the lumen completely.

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<sup>4</sup> Stewart, H. L., and Cantarow, A. Decompression of the Obstructed Biliary System of the Cat. *Am. J. Digest. Dis. & Nutrition* 2: 10 (1935).

clusions completely, for reasons which will presently be given. Nevertheless, there remains much to make his work of physiologic importance.

In the first place, Rous assumed conditions to be simpler than those actually met in practice in that they are applicable only to the bile that is free from infection. Furthermore, the green system of Rous requires a gallbladder that is normal at least functionally. Considering the intimate relationship of all organs, it is difficult to imagine that ligation of the common duct does not have some effect on the normal functioning of the gallbladder.

If the gallbladder is to prevent the production of white bile by means of its concentrating effect, the hepatic bile, of course, must come into contact with the wall of the gallbladder. However, it is doubtful that this takes place in obstruction of the common duct. It is a common observation that during aspiration from the gallbladder or bile ducts there may be a change from a colorless to a colored fluid or vice versa. This indicates how little tendency there is for mixture of the contents of different parts of the biliary system.

In determining whether or not white bile will be formed, the concentrating and diluting effects of the gallbladder and ducts may be contributory but are certainly not the determining factors.

The decolorization responsible for the production of white bile is in all probability brought about by another factor, infection, and is merely increased or decreased by the action of the gallbladder and ducts. It would, of course, take a longer time for white bile to be produced in the green system than in the white system of Rous. The longest observation Rous made on any dog with the green system of Rous was for forty-four days. In my own experiments the shortest time for white bile to appear was in four and one-half months.

Thus, by a combination of the physiologic observations of Rous, Kausch and Bernhard and others and my own experimental results, I have arrived at the following conception of the manner in which white bile is produced.

In the closed system produced by obstruction a long-lasting infection of sufficient virulence produces a decolorization of the stagnant fluid in the gallbladder and bile ducts. It is the original green bile that is acted on and is directly responsible for the production of the colorless fluid. It is entirely possible that a small amount of secretion from the bile ducts may be mixed with this fluid, but in this closed system there certainly is not enough space for any great amount of such secretion to accumulate.

The gallbladder may play a great rôle in determining the time necessary for the decolorization to take place. A gallbladder that is func-

3 Necrosis of the adenomatous processes in the mucosa of the large ducts occurred as early as an hour and a half after decompression, the regressive changes becoming more marked as time went on

4 Atrophy and final disappearance of the newly proliferated ducts occurred as the result of regeneration of the hepatic cells

The necrotic changes in the liver cells reported by Stewart and Cantarow were duplicated in our own experiments, but their other findings were not, and the discrepancy was at first disconcerting. Second thought, however, gave us the explanation. In our experiments the obstruction was released by the creation of an external biliary fistula, which is analogous, it should be noted, to the procedure that would be carried out clinically. In their experiments, on the other hand, the obstruction was released merely by the release of the ligature on the common bile duct, which had not been divided, as it had been in our experiments. The type of procedure that they employed does not reproduce the clinical and pathologic conditions usually found, and the changes which followed it, therefore, would scarcely be observed after a different type of operation.

We made no observations of the kidneys in this series of experiments. Previous clinical and experimental studies have convinced us that the renal changes are the second stage of the syndrome. Since even the first stage was not produced in these experiments, there seemed to us to be small point in wasting time seeking for the second.

tionally intact and in complete connection with the duct system exerts a concentrating effect and thus lengthens the time necessary for the decolorizing process. On the other hand, if the gallbladder is separated from the duct system either anatomically or functionally, the decolorization will take place much sooner. It might be worth while to mention again at this point the fact that the foregoing considerations apply only to the colorless fluid found in the closed system.

*Relief of Obstruction*—Relief of the obstruction immediately brings into play an entirely new set of circumstances. The next problem here is to investigate the colorless fluid often obtained from the common duct several days after relief of obstruction. As in the case of the closed system, one must determine the nature of the fluid obtained as well as its origin and the manner of its production.

In this connection it will be of special importance to understand the rôle played by the liver in producing white bile. The experimental work alone does not yield sufficient information on this point, since only the anatomic picture of the liver is available. No accurate correlation can be made between the anatomic appearance of the liver and its functional capacity. It is a well known observation that a liver with its parenchyma in poor anatomic condition may produce normal-appearing bile.

Another method of approach is the study of actual cases that have shown white bile in man, in which operation has brought about relief of obstruction and in which the resulting secretion is observed by means of a fistula for a definite period. Walters and Greene, as well as Andrews, have described a few such cases of relief of obstruction of the common duct. These authors agreed in reporting that after operation for obstruction the bile gradually changes from white to colored but that the immediate effect of the relief is the production of a greater quantity of white bile than was produced during the course of the obstruction. This cannot properly be called a colorless hepatic secretion, since the pigment content of the liver and the general jaundice present at this time bear witness to the fact that the hepatic cells are still producing bilirubin. Furthermore, one would hardly expect the character of the hepatic secretion to change from white to green within a short time. This change has often been observed to take place within a few hours, while in the case reported by Judd, mentioned previously, the bile changed from white to green immediately following the relief. It is probable that during the obstruction the bilirubin either is retained in the hepatic cells or is released into the blood stream. After relief of the obstruction this bilirubin might gradually make its way through the damaged biliary capillaries and produce a change to green bile.

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## COMMENT

Thus it seems that the secretion of the liver plays no part in the production of the colorless fluid drained from the common duct after relief of obstruction. There must be another origin for this fluid.

The only other possibility is that this fluid is a secretion of the mucous membrane of the ducts and is therefore very different from the colorless bile of the closed system. Unfortunately, this cannot be proved chemically, since both mucus and leukocytes are found in each case. Mucous secretion from the glands of the bile ducts undoubtedly plays some rôle in the closed system, too, as mentioned previously. Relief of the obstruction simply allows this secretory process of the ducts to take place unopposedly. On the other hand, the operation for relief of obstruction may either act as an inflammatory stimulus to the mucous membrane of the ducts or cause the recurrence of an old inflammation. Either factor would produce an increased quantity of colorless secretion for a few days. This fluid gradually becomes colored as a result of the activity of the liver which mixes its pigment with the colorless fluid.

## SUMMARY

Eleven dogs were used for the experimental work, which consisted of ligation of the common duct followed four weeks later by injection of bacteria into the biliary system. This procedure resulted in the appearance of white bile in four dogs.

In comparing the cases in which white bile appeared with those in which the bile remained unchanged, it is seen that the fundamental factor in the pathogenesis of white bile is the presence of infection. Infection accompanying obstruction of the common duct must be present for a long time and must be of sufficient virulence. The beginning of decolorization was demonstrated after thirty-two days, while completely white bile appeared after four and one-half months. The most effective organism for bringing about this infection seems to be *B. coli*.

In discussing the pathogenesis of white bile a sharp distinction is made between white bile found in the closed biliary system and the colorless fluid obtained from the open system after relief of obstruction.

In the closed system infection brings about a transition of the originally green bile to white bile. This decolorization is brought about by the leukocytes, which appear as a result of the bacterial stimulus. They absorb the bile pigment and carry it off. A small amount of secretion from the mucous membrane of the ducts is subsequently mixed with this colorless fluid. Quantatively, however, this plays a minor rôle.

As a result of the relief of obstruction the white bile is swept out of the bile ducts. For a few days an increased quantity of colorless fluid is obtained, which is shown to be the secretion of the mucous mem-

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brane of the ducts. Since this secretion has nothing to do with hepatic bile, to apply to it the name of white bile would be misleading. Here again infection seems to play some part in the production of the colorless fluid. It is highly probable that the operation for relief of obstruction causes an increased secretion by acting as an inflammatory stimulus to the mucous membrane of the ducts. Gradually the liver assumes its normal function if it has not been too severely damaged anatomically.

In addition there are reported four clinical cases in which white bile was found, these constituting 15 per cent of the total number (twenty-six) of cases in which operation for obstruction of the common duct was performed at the University of Chicago Clinics during the last five years. This relatively high percentage can be explained by the fact that these statistics include cases in which the presence of white bile was discovered only on chemical examination. In these four cases the clinical history, the findings at operations and in one case the post-mortem examination revealed signs of long-lasting infection accompanying obstruction of the common duct. Two cases of long-lasting obstruction of the common duct are reported in which neither clinically nor at operation were there any signs of infection. In both cases deep green bile was obtained.

The histories of the clinical cases reported agree with the histories cited in the American literature in indicating the prognosis in cases of white bile to be serious but not hopeless.



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# THE SO-CALLED "LIVER DEATH"

AN EXPERIMENTAL STUDY OF CHANGES IN THE BILIARY DUCTS  
FOLLOWING DECOMPRESSION OF THE OBSTRUCTED  
BILIARY TREE

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AND

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NEW ORLEANS

In previous communications on this subject<sup>1</sup> we have discussed two separate phases of the so-called "liver death" or "liver-kidney syndrome"

We have analyzed thirty-four cases of this syndrome described in the records of the New Orleans Charity Hospital in the seven year period terminating on Dec 31, 1934. In twenty-three cases the syndrome followed operation on the biliary tract, in four it followed surgical treatment for acute pancreatitis, and in seven it was associated with trauma to the liver.

We have reported a series of experiments, ten in all, in which we endeavored to reproduce in laboratory animals the clinical and pathologic processes which we had observed in human patients. Two experiments were successful.

In the first experiment, the biliary tree was obstructed for from twelve to twenty days (by ligation and division of the common bile duct and cholecystectomy), at the end of which time the obstruction was released and an external biliary fistula was created. In every instance after the decompression there was a prompt decrease in the jaundice, followed almost immediately by increasing listlessness, anorexia without gastro-intestinal symptoms, and oliguria which rapidly progressed to anuria. Death occurred in from seventy-two to ninety-six hours in all the animals which were not killed when their state was clearly terminal. Urinalysis showed albumin, casts and red blood cells, and in five instances the previously normal nonprotein nitrogen content of the blood rose to 72, 81, 93, 105 and 171 mg, respectively. In all the dogs autopsy showed degenerative changes in the liver cells and in the convoluted tubules of the kidneys typical of the lesions exhibited in cases of liver-kidney death in human patients.

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From the Department of Surgery of the School of Medicine of Louisiana State University

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In the second experiment, precisely similar clinical symptoms and postmortem hepatorenal changes followed the injection into the animals of saline and aqueous extracts made from the liver of a patient who died with the typical syndrome of hyperpyrexia characteristic of liver death after cholecystectomy, the alcoholic extract did not reproduce the picture. Autopsy on this patient had ruled out hemorrhage, leakage of bile, peritonitis, embolism and pneumonia and had revealed marked necrosis of the liver cells. The urine of these animals revealed albumin, casts and red blood cells, but determinations of the chemical composition of the blood, unfortunately, were not made, since the experiment was one of the first done and its full significance was not realized.

On the basis of this clinical and experimental evidence, we have evolved the following theory to explain the occurrence of this highly fatal complication.

1 The same symptom complex is apparent and the same underlying factors are operative in the various conditions studied (postoperative biliary disease, postoperative pancreatic disease and hepatic trauma), and we believe, on the basis of a casual survey of unselected autopsy reports in cases of disease of the thyroid gland, burns and intestinal obstruction, that this same syndrome may develop in these and perhaps in other pathologic states in which it has not yet been identified.

2 The underlying factor is some degree of hepatic damage which either is preexistent or is the result of direct trauma. In the former circumstances the damage is not incompatible with the strain of normal life, but it is incompatible with the added strain incident to surgical intervention. The chain of events following hepatic trauma is the same, except that the damage is abruptly produced and is not of gradual development as it is in diseased states.

3 When such a strain is superimposed on the existing hepatic disability, the damaged liver cells, failing in their function, release into the circulation some potent toxic substance, which, on the basis of our experimental evidence, seems to be water soluble.

4 This substance, circulating in the blood, is excreted by the kidneys through the convoluted tubules, and they, unfitted by nature for such a load, promptly break under it.

5 The two types of liver death originally described by Charles Gordon Heyd<sup>2</sup> we consider to be a single pathologic process. Our evidence indicates that cases in which sudden death occurs with hyperpyrexia and in which only hepatic changes are apparent at autopsy represent the first stage of the process which terminates in deferred death from uremia, in which renal as well as hepatic changes are apparent at autopsy.

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<sup>2</sup> Heyd, C. F. Liver and Its Relation to Chronic Abdominal Infection, *Ann Surg* 79:55 (Jan) 1924.

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The clinical and experimental evidence which we ourselves have adduced corroborates the suggestion made by other writers on the subject, notably Helwig, Schutz and Kuhn<sup>3</sup> that the toxin postulated in our theory is produced in the liver cells, in which, it is generally agreed, the first damage occurs

Both positive and negative proof is necessary to establish this theory On the positive side, the toxic substance must be isolated from the damaged liver cells, and this we are attempting to do at the time of writing On the negative side, it must be proved that it does not originate elsewhere in the biliary system, and with that proof this communication is concerned

If the toxin in question should be produced anywhere in the biliary system except in the damaged liver cells, the most reasonable place would be the tissues lining the biliary ducts These ducts, especially if

TABLE 1—Results of Simple Obstruction of the Biliary Tree in Six Dogs Which Were Used as Controls

Dog	Procedure	Duration of Obstruction, Days	Observations
9	Ligation and division of the common duct	4	Not significant
14	Ligation and division of the common duct cholecystectomy	6	Not significant
16	Ligation and division of the common duct cholecystectomy	18	Very slight flattening of the epithelial cells lining the small and medium sized ducts
17	Ligation and division of the common duct cholecystectomy	20	Not significant
18	Ligation and division of the common duct, cholecystectomy	20	Not significant
4	Ligation and division of the common duct	36	Slight flattening of the epithelial cells, as in dog 16

the gallbladder has been removed, are the only structures other than the liver cells which feel the effect of biliary stasis In order to make certain that they are not implicated in the production of the toxic substance, we undertook a series of experiments in which we studied the effect on them of decompression after obstruction and in which we studied, as a control, the effect on them of simple obstruction

Our report, after the elimination of the dogs which died of infection and of other causes after experimental obstruction of the biliary tree, concerns twelve dogs In six animals, which were used as controls, obstruction was done and was not released, in the other six decompression of the obstruction was done from four to thirty-six days after the obstruction had been produced

3 Helwig, F, and Schutz, C B A Liver Kidney Syndrome, Surg, Gynec & Obst 55 570 (Nov ) 1932 Schutz, C B , Helwig, F C, and Kuhn, H P A Contribution to the Study of So-Called Liver Death, J A M A 99 633 (Aug 20) 1932

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nected with the anesthesia. But in spite of the confusing factors, study of this type of headache has yielded certain results. In the first place, no matter what area is anesthetized or for how long, it is always the head that aches. The localization of the discomfort is vague and inconstant, even in the same patient, but there is never any doubt as to its being in the head. I see no way to interpret this except as a disturbance of the hydrostatics of the cerebrospinal system.

The second point of interest which emerges is the precise uniformity of the time of appearance. I have observed cases in which anesthesia

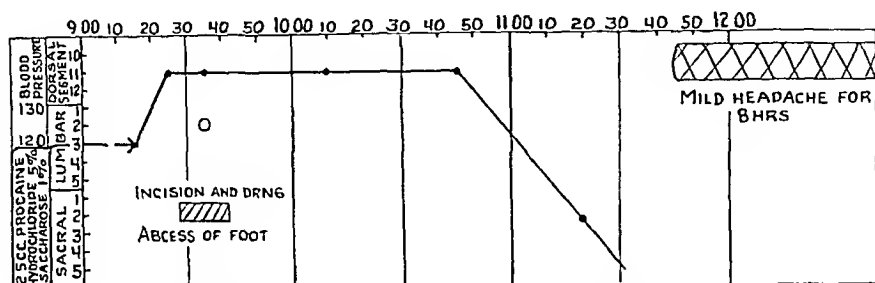


Fig 2—A typical headache appearing immediately after disappearance of the anesthesia in an Arab Bedouin aged 35. He was up and about after the operation. He would probably have felt no headache if he had remained recumbent. His general condition was good.

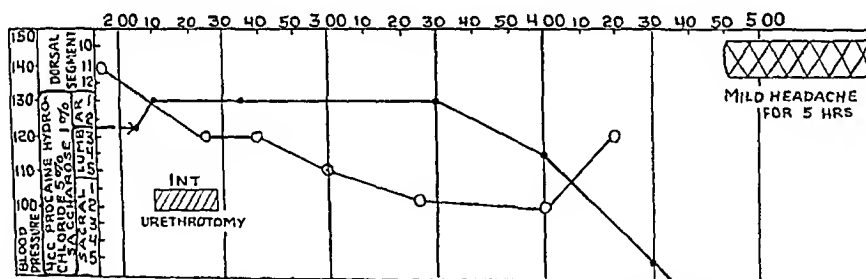


Fig 3—A typical case, with headache appearing immediately after the disappearance of the anesthesia. The patient was in good general condition.

with nupercaine lasted six and even eight hours, but I have never observed a case in which headache appeared during the course of the anesthesia. It always starts a short time after the disappearance of the anesthesia. This is a uniform finding whether the anesthesia lasts for thirty minutes or eight hours and whether it involves the fourth and fifth sacral segments only, as is usual in cases in which hemorrhoidectomy is performed, or extends to the third dorsal segment, as is required for a splenectomy. Figures 2, 3 and 4 illustrate this uniformity of appearance under varying circumstances.



I observe an occasional case in which no headache is felt but in which at the time when headache would occur other sequelae are experienced. Figures 5 and 6 are charts for such cases.

The uniform appearance of the headache immediately after the disappearance of the anesthesia strongly suggests that there is a vasomotor reaction. Spinal anesthesia abolishes the tone of the blood vessels in the extremities, a fact used in the study of Buerger's disease and allied

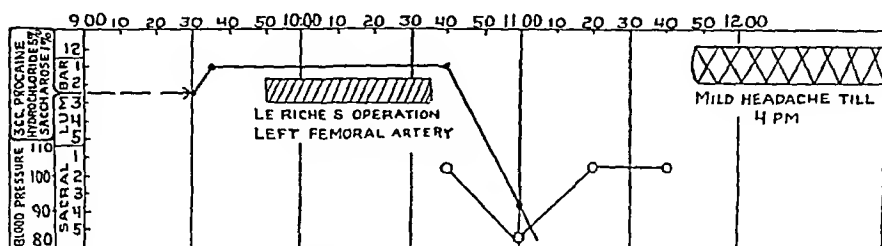


Fig 4—A typical case of headache appearing immediately after the disappearance of the anesthesia in an Arab woman aged 30 with Buerger's disease. She was in very bad general condition and died a few days later, after amputation of the leg.

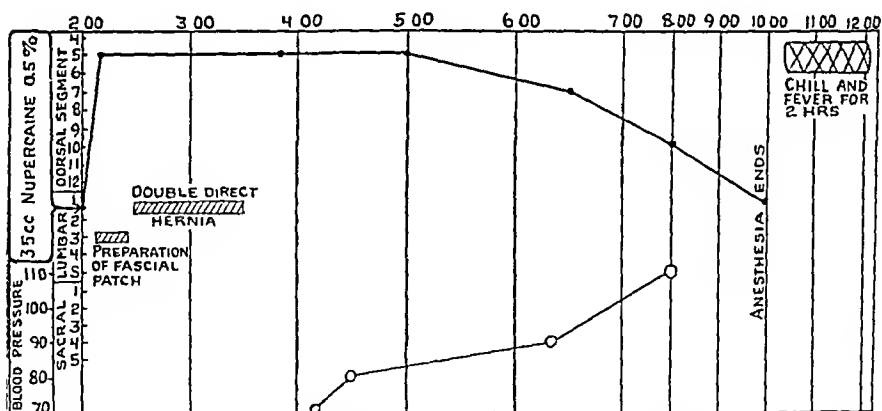


Fig 5—A case of prolonged nupercaine anesthesia in a Persian stoic aged 70. Even after such a long anesthesia the postanesthetic disturbance appeared immediately after the disappearance of the anesthesia. No headache was experienced in this instance, but fever was ushered in by a mild chill and lasted two hours.

troubles. It would seem certain that a similar result must be produced on the vessels of the meninges and the cord and that throughout the time of spinal anesthesia the vessels are toneless and dilated over the area bathed by the anesthetic solution. On the disappearance of the anesthesia vasomotor control of these vessels is reestablished, and at this point the headache appears.

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diminished secretion of cerebrospinal fluid or to its accelerated absorption from the subarachnoid space. The fluid is secreted by the choroid plexuses, and they are far removed from the influence of the injected anesthetic. That would seem to leave as the one remaining obvious possibility an accelerated absorption of the cerebrospinal fluid and, resulting from that, a persisting condition of abnormally low intra-arachnoid pressure.

It seemed possible to test some points in this analysis, and for this purpose we had made up ampules of the nonirritating solution previously described, to which had been added minute doses of ephedrine ( $\frac{1}{25}$  grain [0.0026 Gm]) and epinephrine ( $\frac{1}{6}$  minim [0.0124 cc]) respectively. The results were interesting and seemed to confirm the impression that in headache resulting from spinal anesthesia more than one factor is involved. With these solutions headache did not appear

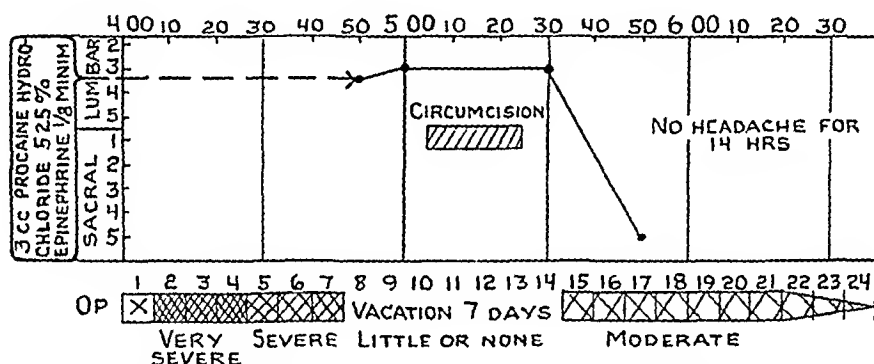


Fig 7—The delay in onset of headache when a trace of epinephrine was added to the injected anesthetic occurred in a large powerful Portuguese aged 40. This is a uniform result after the addition of either ephedrine or epinephrine. The onset occurred fourteen hours after the disappearance of the anesthesia. The headache was mild for one day, and was felt only when the patient shook his head. The headache was very severe for the following three days and fairly severe for the next three. The patient kept steadily at work in his office. A vacation of a week brought much relief, but the headache recurred when he resumed work and persisted for another week, after which it gradually disappeared. Cases of ambulant patients such as this are the severest test of spinal anesthesia. This man would have been far better off to have undergone short general anesthesia for such a minor operation as circumcision.

immediately after the disappearance of the anesthesia but followed a period in which the patient was free from all complaint. This free period usually lasted about twelve hours, though it was sometimes much longer. Unfortunately when the headache appeared it seemed to be undiminished in severity, i. e., negligible if the patient remained recumbent but sometimes severe if he walked about. Figure 7 is a good illustration.

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and the clinical picture was ambiguous. I turned then to the use of solutions of dextrose. They are widely used in various conditions of low blood pressure, and their effect is fairly lasting. As the present routine procedure 4 ounces (124.4 Gm.) of 5 per cent dextrose in physiologic solution of sodium chloride is injected immediately following the operation. This introduces the dextrose solution at different times in the course of the anesthesia, but I have not been able to see that the result is thereby affected. Figures 8, 9 and 10 are charts for such cases.

This procedure was a surprising success and has very nearly stopped the study of headache. One patient admitted on questioning that he had a little headache. With that exception the material for study disappeared. My own interpretation of this result is that the anesthetic solution, even as nonirritating as I have been able to make it, still injures the delicate pia-arachnoid sufficiently to cause excessive absorption of cerebrospinal fluid and that this causes the headache which has been so troublesome. The slight hydremia which the dextrose solution induces is sufficient to check this excessive absorption until recovery or, probably, until compensation can take place, thereby reducing the disturbance in cerebrospinal hydrostatics to so low a level that headache does not appear.

#### SUMMARY

By using anesthetic solutions carefully made up to be as nearly nonirritating as possible, postanesthetic headache is reduced almost to the point of disappearance in patients in the recumbent position.

By means of the intravenous injection of 4 ounces of a 5 per cent solution of dextrose in physiologic solution of sodium chloride immediately after the operation headache is largely prevented even in ambulant patients.



loss of control of the bladder and the bowels. Marked sensory disturbances were also noted. In addition, the patient stated that the mass in the region of the right flank had shown rapid growth during the past year.

*Examination*—The patient, an emaciated man of 21 years, was of fairly normal height. The skin in general was dark, but on it, especially on the dorsal aspect of the trunk, were scattered many dark brown pigmented spots varying in size up to several inches in diameter. These were not elevated.

A striking feature was an enormous tumor on the right flank (fig 2), about the size of a man's head, roughly spherical and covered with intact though



Figure 1



Figure 2

Fig 1—The patient as he appeared in March 1924. The kyphoscoliosis and cutaneous pigmentation are evident. The elephantiasic skin flap can be seen in the right gluteal region. The tumor on the right flank can be made out.

Fig 2—The patient in 1934. The tumor shows considerable growth, as does the elephantiasic skin flap below it.

atrophic and pigmented skin. The subcutaneous veins were distinctly enlarged. The lower half of the tumor was hard but showed smaller areas of varying consistency. The upper half was more elastic and in some areas gave the impression of fluctuation. Below the tumor an extremely large hyperplastic skin flap pre-

This reestablishment of vasomotor control must inevitably involve some disturbance in cerebrospinal hydrostatics, for with it must come a shrinkage in the volume of the vessels and thereby a slight increase in the space to be occupied by the cerebrospinal fluid. With this must occur a slight drop in the intra-arachnoid pressure. The obvious objection to this analysis is that the changes in volume accompanying this reestablishment of vasomotor tone must be exceedingly small, and a priori one would suppose that such minute changes could be easily compensated for by the elasticity of the dural sac. Moreover, even in the cat the cerebrospinal fluid is secreted at a rate of about 12 cc a day<sup>6</sup>. In man the figure must be much higher. Any deficit in cerebrospinal

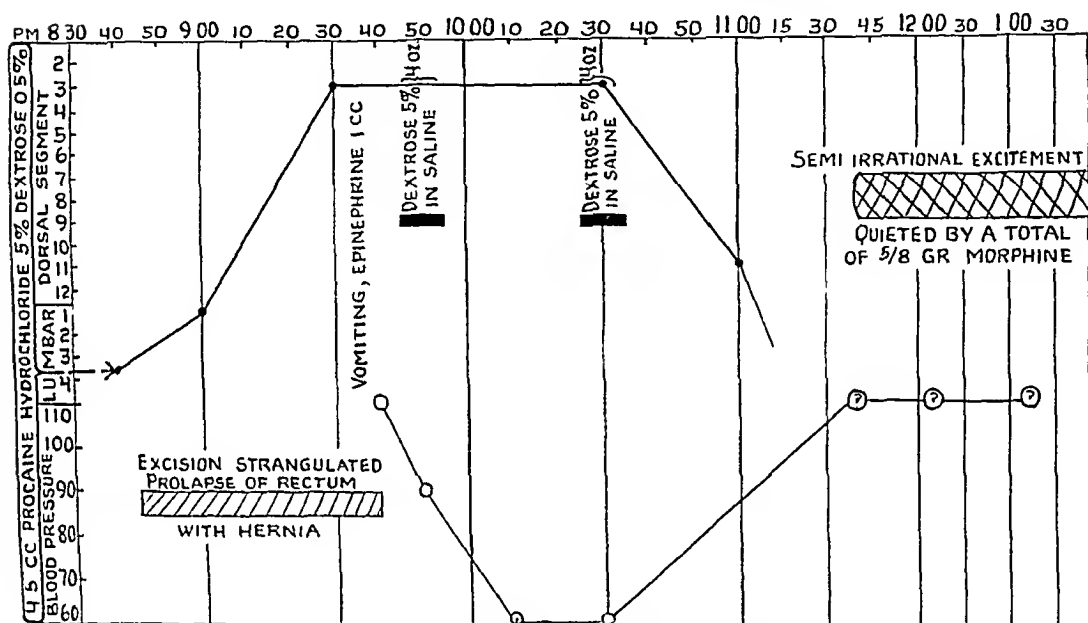


Fig 6—The patient, a Beloochi aged 50 of somewhat unstable mentality, was in a very toxic condition. His position on the table was disarranged and resulted in anesthesia of the upper segment. Artificial respiration was administered once and epinephrine once. Dextrose solution was given twice, making a total of 8 ounces. No headache appeared, but a period of irrational excitement followed immediately after the disappearance of the anesthesia. The patient spent this period walking about in the compound of the hospital.

fluid could be made up in a few hours at the longest, whereas the headache sometimes lasts for days.

This would seem to necessitate the conclusion that even though the inception of a postanesthetic headache may be due to a slight drop in intra-arachnoid pressure accompanying the reestablishment of tone in the previously anesthetized vessels, its continuance must be due either to a

6. Weed, Lewis. Personal communication to the author.



scoliotic element. The vertebral bodies were porotic and collapsed and owing to the destruction of the intervertebral disks could not be differentiated from each other at the apex of the curve. In addition, deformity of the ribs was apparent.

Neurologic examination revealed a narrow, circumferential area of hyperesthesia around the trunk, below which hypesthesia and anesthesia involving all of both lower extremities was present. There was absence of tactile sensation and of the ability to distinguish between heat and cold. Motor paralysis of the bowels and bladder and of both lower extremities was complete. There was ataxia distally but not proximally. There was absence of the tendon reflexes.

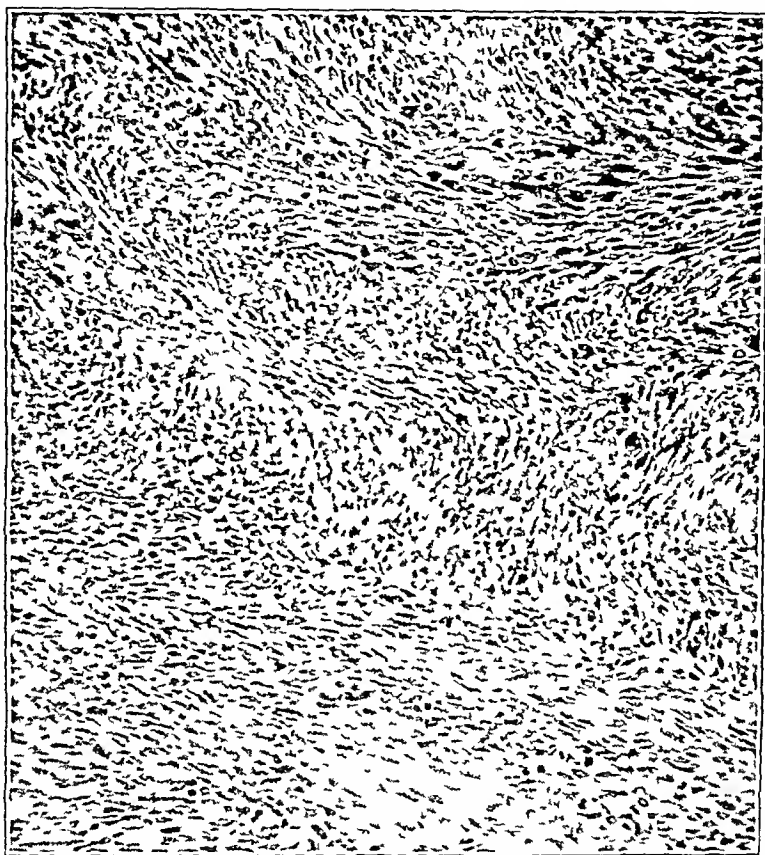


Fig. 4—A medium power photomicrograph of the large tumor, showing spindle cell sarcoma with bundle formation.

The findings were typical for transverse myelitis beginning at the level of the first lumbar vertebra, the apex of the kyphoscoliotic curve.

*Operation*—Because of the patient's poor general condition a laminectomy seemed inadvisable. However, an operation was performed to obtain a specimen for biopsy to determine whether the tumor was malignant. It was found that the large mass and the adjoining smaller ones could be easily enucleated though there was invasion of the fascia lata of the gluteal and tensor muscles. Huge ramifying nerve trunks were found to enter and adhere to the tumor. In spite of the slight degree of trauma at operation, shock ensued, and the patient died in a few hours.

I experimented with the intravenous injection of distilled water in the hope that an abnormal amount of water in the blood might stop excessive absorption of cerebrospinal fluid into the blood stream. The distilled water probably does have that effect, at least for a time, but it

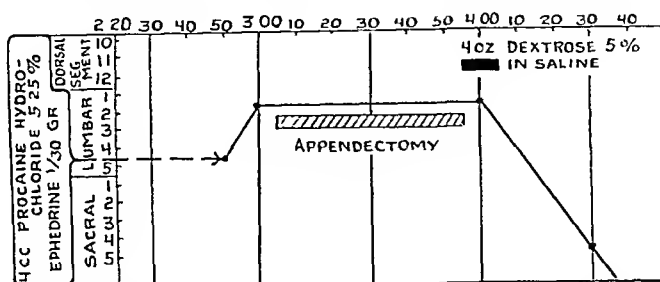


Fig 8—The patient, an Arab aged 30, gave a typical reaction following an intravenous infusion of dextrose as a prophylactic against headache. No headache occurred at any time.

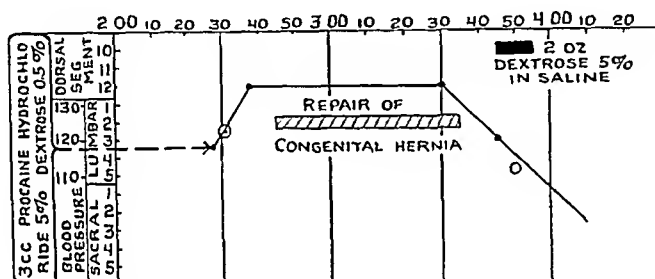


Fig 9—A typical reaction following prophylactic infusion of dextrose solution. The patient was an Arab boy of 10 years in poor general condition. He was put under no restraint, and sat up a large part of the time. No headache occurred at any time. He was able to sit up immediately after the operation.

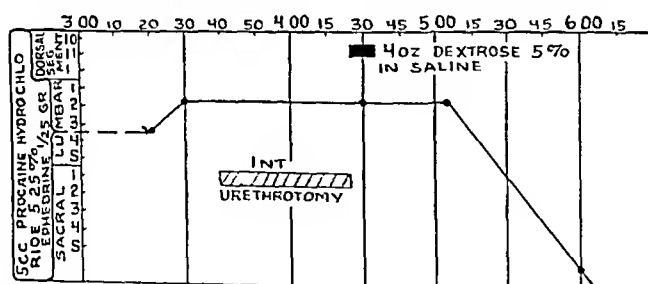


Fig 10—The maximum degree of headache following a prophylactic injection of a solution of dextrose. The patient received 5 cc of a 5 per cent solution of procaine hydrochloride, which is the maximum dose in the Muscat clinic. He was up and about immediately following the operation. He made no complaint but on questioning admitted that he had some headache. He required no medication.

produces headache and fever on its own account and is used for that purpose in protein shock therapy. The results were unsatisfactory,

enclosed in a perineurium, which was also thickened. Normal nerve fibers were not evident. The vessels, though large, were of normal structure.

Beneath the capsule the living tissue was arranged in fibrous bundles (fig 4). The structures were edematous and hyperemic. Under high power magnification the picture of a benign lesion was quickly dispelled. Among the more numerous fibrocytes were a number of smaller cells which were richer in chromatin and contained nuclei showing all the stages of mitotic division. The absence of a necrobiotic zone between the living and the dead tissue (fig 5) and the presence of large areas which had become necrotic but still showed structural detail evidenced the rapidity of the growth of the tumor, with which the blood supply was unable to keep pace. Still further regression was seen in other areas, with



Fig 6—A section through the large tumor, showing colliquation resulting in the formation of a cyst with a good fibrous capsule.

complete destruction of the tumor tissue and the formation of cysts (fig 6). In other places extensive hemorrhage by diapedesis and rhexis was evident.

The six smaller tumors removed were roughly of the size and shape of a hen's egg and showed thickened fibrous bands entering and leaving the poles. These tumors were hard and fibrillated, with areas of central necrosis which with a yellow sulfur-like stain suggested grossly *mollusca fibrosa* in different stages of catabolism. The fibrous bands consisted of nerves with marked proliferation of the interstitial and perineural connective tissue. In one of these tumors an angioma was present. All showed signs of early malignant degeneration (fig 7). The yellow stain was imparted by the presence of huge cells which had foamy protoplasm and contained lipoid substance (fig 8).

# NEUROFIBROMATOSIS

WITH REFERENCE TO SKELETAL CHANGES, COMPRESSION MYELITIS AND MALIGNANT DEGENERATION

ALEXANDER MILLER, M D

CINCINNATI

In its simpler form the typical pigmented spots on the skin and the multiple small subcutaneous nodules render neurofibromatosis easily recognizable. These characteristic changes, however, are not always present and at times are so overshadowed by other extensive and bizarre pathologic changes involving both the soft and the bony tissues that confusion in diagnosis may readily result. Numerous cases already reported illustrating interesting changes of the skin, subcutaneous tissues, nervous system and skeleton, extend considerably the knowledge of the disease described by von Recklinghausen in 1882. To these a case of extensive involvement of the vertebral column leading to compression myelitis, with sarcomatous degeneration of more than one neurofibroma seems worth adding.

## REPORT OF A CASE

*History*—H. M., a white boy aged 11 years, first came under observation in this department on March 12, 1924. The complaint was curvature of the spine, first noticed at 1 year of age, with a gradual increase in the deformity. In addition, a mass in the left inguinal region of several years' duration was noted. A history of the patient's birth, development and family revealed nothing unusual.

Physical examination revealed severe kyphosis (fig 1) of the lower portion of the dorsal segment and the upper portion of the lumbar segment of the spine, with moderate scoliosis to the right and marked tilting of the pelvis. Over the posterior aspect of the right os ilium a typical elephantiasic skin flap about the size of a silver dollar was present. In the left inguinal region a similar formation was seen. The skin showed many pigmented spots characteristic of the disease. These had been present since birth.

Treatment for the kyphoscoliosis was instituted and the patient was followed up for a period of five years, during which time little change in his condition was noted. He was not seen for several years, until he returned in July 1933 for a new brace. At this time he did not complain of unusual disability or discomfort and stated that he had been doing farm work. An increase in the spinal deformity, however, was noticeable.

The patient was not seen again until April 1934, when he was admitted to the hospital because of inability to walk. Six weeks previously some pain had been noticed in the region of the back. A week later the left leg felt numb and weak, and the next day the right leg became similarly involved. Three days later paralysis of both legs became complete, and this was followed the next day by

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The sections through the elephantiasic skin flap (fig 9) showed marked fibrosis of the subcutaneous layer, with some attempt at the formation of bundles. The fibrous tissue was dense and almost hyaline. Where looser and more cellular tissue was present, peripheral nerves could be seen. These had undergone pathologic change and showed fibrous proliferation similar to that previously described. The sweat glands, in addition to being more numerous, were hyperplastic, owing



Fig 9—A section of the elephantiasic skin flap, showing fibrous proliferation of the subcutaneous layers, with thickening of peripheral nerve ends

to an increase in connective tissue stroma similar in structure to that of the perineurium.

On histologic examination papillae in the skin were not seen. The epithelial layer showed little change except for a great amount of brownish granular pigment occupying the basal cell layer. The skin over the tumor was essentially normal except for areas which showed hyperpigmentation, chiefly in the stratum Malpighi but occasionally in the corium.

senting the characteristic appearance of elephantiasis covered the entire right gluteal region. Through this, several small tumors of the size and shape of a hen's egg were palpated. Their longitudinal axes ran parallel to the leg, and thick fibrous strands could be felt emerging from the poles.

A huge gibbous formation beginning at the eleventh dorsal vertebra and with its apex over the first lumbar vertebra was another prominent feature. There was some deviation of the spine to the right. The lumbar portion of the spine could not be made out distinctly, owing to the degree of kyphosis, but marked lordosis with rotation of the spinous processes to the right seemed to be present. The lower ribs were in contact with the iliac crest on the left side. Over the lower portion of the spine a circumscribed area of hypertrichosis was present in the midline.

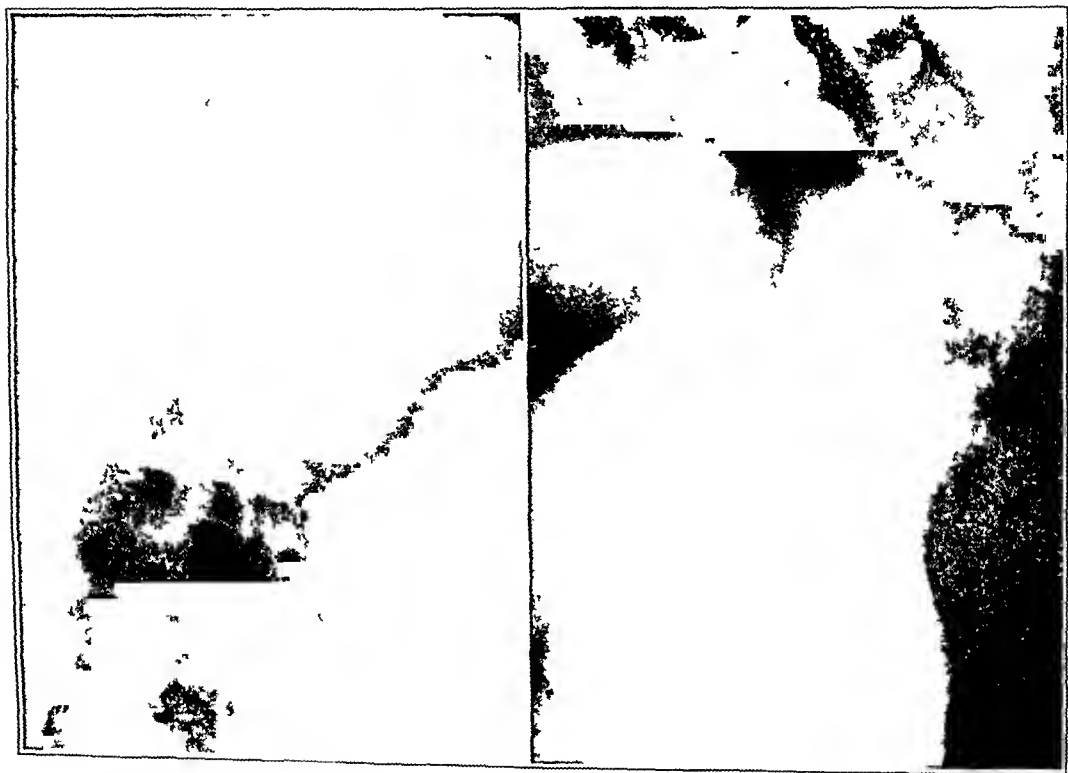


Fig 3—Anteroposterior and lateral views of the vertebral column, showing kyphoscoliosis, osteoporosis with compression of the vertebral bodies and deformity of the ribs.

The elephantiasic skin flap in the left inguinal region was firm and gave the impression of a hard fibroma. A small spindle-shaped tumor was visible on the outer side of the right wrist. Several small movable fibromas were palpated along the intercostal nerves. Palpation of the larger nerve trunks did not reveal other growths. The inguinal lymph nodes on the right side were enlarged.

The anteroposterior and lateral roentgenograms (fig 3) showed a severe curvature involving the lower portion of the dorsal segment and the upper portion of the lumbar segment of the spine. Sharply hooked kyphosis with the apex at the first lumbar vertebra could be seen to which was added a somewhat milder

creates a disposition for the later appearance of osteitis fibrosa a supposition which seems groundless With periosteal hyperemia thickening of the bone may follow (Weber<sup>4</sup>)

In addition to the circumferential changes, abnormalities in the longitudinal growth of bone have occasionally been reported When irritation is present, usually in areas where elephantiasis or plexiform neuromas are situated, an increase in the length of the bone may occur This hyperplasia may reach the extent of gigantism, usually of a single extremity Should decreased vascularization of the epiphyseal plate result, a shortened hypoplastic extremity may be expected Such a hypoplastic extremity was present in one of Brooks and Lehman's cases as the result of destruction of the epiphyseal plate by a subperiosteal cyst

These same processes of atrophy and hypertrophy and of hyperplasia and hypoplasia may involve the bones of the trunk with resultant deformities and displacements, disturbances of growth and structural changes of the ribs and the pelvis Here, also, may be found porosis formation of cysts and areas showing bony defects

Most frequent of all the changes in bone in cases of neurofibromatosis are those involving the spinal column In about 43 per cent of the cases in which skeletal changes occur, the vertebral column is affected The deformity is fairly characteristic and consists of kyphoscoliosis which differs in several important details from the usual types of scoliosis or kyphosis The site of predilection is the lower portion of the dorsal segment of the spine The deformity may first be noticed in early childhood The kyphotic element strongly predominates while the scoliosis is slight and presents a moderate degree of rotation A typical feature is the presence of a sharp kink at the apex of the gibbus Here a deep abrupt step may be seen and is palpable, so that the upper portion of the kyphotic part of the spine seems to overhang the lower part (fig 1) The apex of the curve lies usually in the midline, and just below this point the rotation of the spinous bodies is most noticeable

The cause of this collapse of the vertebral column with at times a resultant dwarfism, has been variously explained Gould<sup>5</sup> expressed the opinion that softening of the bone occurs which microscopically and macroscopically is indistinguishable from osteomalacia In cases of neurofibromatosis, however, the loss of calcium salts is not so great as in those of the malacic disease Other observers also have remarked on the similarity of the pathologic picture in the two conditions Though

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4 Weber, F Parkes Periosteal Neurofibromatosis with a Short Consideration of the Whole Subject of Neurofibromatosis, *Quart J Med* **23** 151 (Jan) 1930

5 Gould, E P Bone Changes Occurring in von Recklinghausen's Disease, *Quart J Med* **11** 221 (April) 1918

*Biopsy*—The large tumor measured 10 by  $\frac{1}{2}$  by 5 inches (25 by 12 by 12 cm), weighed  $7\frac{1}{2}$  pounds (34 Kg) and was covered with a dense fibrous capsule except at the base, where the mass was torn and necrotic tumor tissue was present. The nerves entering the tumor were thickened and fusiform and on cross-section did not show definite nerve fibers. The tumor varied in consistency, and irregularly distributed in it were several cystlike formations containing a dark fluid. On section the tumor was seen to be edematous, complex, grayish white at the periphery and hemorrhagic in the central portion. Colliquation



Fig 5—A section through the cellular portion of the large tumor, showing a sharp line between the living and the necrotic tumor tissue. There is evidence of rapid growth with failure of blood supply to keep pace

and necrotic tissue could be distinguished but a grossly malignant condition could not be definitely established. On histologic examination the capsule was seen to be invaded in places by tumor cells and to show round cell perivascular infiltration. Some muscle was adherent to parts of the capsule and in both these structures markedly thickened nerves were present. This enlargement of the nerves reached in some instances five times the normal size and was due to proliferation of the endoneurium



The observations of Jaroschy,<sup>8</sup> Globelski<sup>9</sup> and Valentin and Putschai<sup>10</sup> on the occurrence of paraplegia in cases of severe curvature of the spine are applicable to the case reported here. That the myelitis in the reported cases was due to compression of the cord was proved by laminectomy by the first two investigators and at autopsy by Valentin and Putschai. The syndrome presents a typical picture. Except for the deformity of the spinal column, no cause is apparent. The paralysis develops without pain or fever and progresses rapidly to practically complete myelitis, involving also the bladder and the bowels. The paraplegia is as a rule spastic. The site of the lesion of the cord corresponds to the apex of the scoliotic curve and on roentgen examination of the spinal cord a block can be demonstrated. The dorsal portion of the spine is almost always involved. The paralysis usually sets in in the latter half of the second decade of life, i. e. it corresponds to one of the periods of rapid growth. In 60 per cent of the twenty cases reviewed by Globelski<sup>9</sup> the scoliosis was congenital. Originally compression myelitis was thought to occur in patients with this type of scoliosis only, but later observations showed the occurrence of this lesion in patients with rachitic deformities of the spine. As to the mechanical origin of the lesion of the cord, compression by the kinked vertebral column, by bony or cartilaginous projections into the spinal canal and by torsion of the cord and dura were described by the authors just mentioned. Laminectomy is the treatment of choice and offers a good prognosis for recovery from the paralysis. The dura should be opened because of the torsion frequently present.

Except that the paralysis was of the flaccid type, the condition in the case reported here showed a distinct similarity to the features of compression myelitis associated with spinal curvature. The patterns of clinical history and age were identical and indicated a similar mechanical causation.

Pathologically the principal lesion in neurofibromatosis is proliferation of the endoneurium with hyperplastic changes in the perineurium. The process frequently proceeds to the point where all evidence of nerve fibers is lost. There may be localized thickening of the nerves palpable as small subcutaneous nodules or rather diffuse involvement resulting in the fusiform-shaped strands. The lesions may vary from the small, discrete seed-like tumor to the large, coarse communicating plexiform neuroma. The peripheral nerves are by far the most frequently and

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8 Jaroschy, Wilhelm. Ueber Spatschadigungen des Rückenmarks (Kompressionsmyelitis) bei schweren Skoliosen, *Beitr z klin Chir* **142** 597, 1928.

9 Globelski, M. Kompressionslahmung des Rückenmarks bei Skoliose, *Ztschr f orthop Chir* **57** 220, 1932.

10 Valentin, B., and Putschai, W. Clinical Pathology of Kyphoscoliosis with Damage to the Spinal Cord, *Ztschr f orthop Chir* **57** 245, 1932.

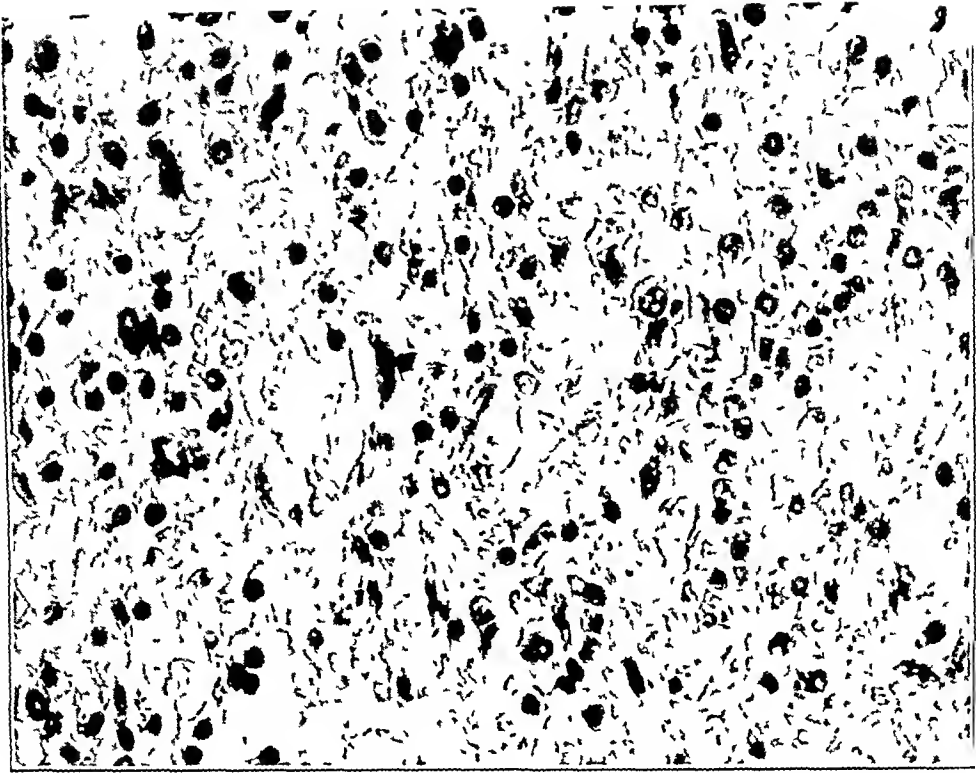


Fig 7—A high power photomicrograph of one of the smaller tumors with anaplasia of cells indicating a beginning malignant process. Each of the six smaller growths showed this picture.

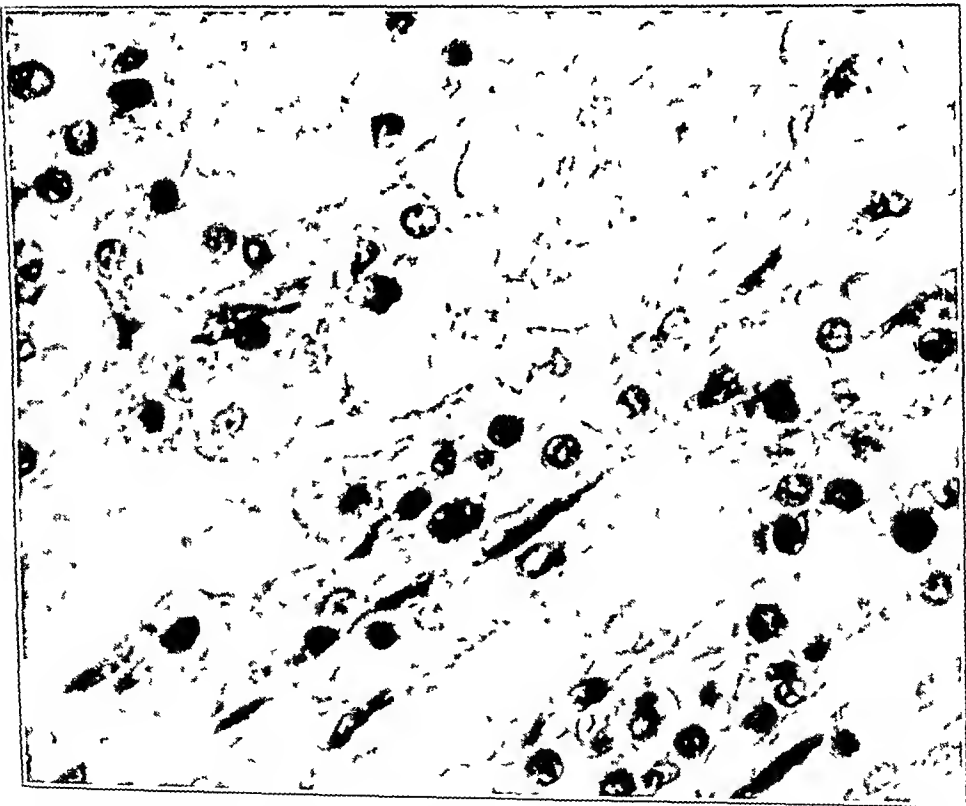


Fig 8—A high power photomicrograph through the yellow-staining portion of a small tumor showing large, foamy cells.

development of such nodules the nerves were probably already undergoing pathologic changes at the time of the original examination, though not yet clinically manifest. In the case reported here the cutaneous nerves underlying the hyperpigmented skin showed fibrosis microscopically, which was indiscernible grossly and which could not have been discovered on clinical examination.

Nothing new can be added concerning the etiology. The preponderance of changes involving the mesodermal tissue, especially the peripheral nerves, the subcutaneous tissue and even the sweat glands, lends further support to the hypothesis that neurofibromatosis is a manifestation of a congenital disturbance of the mesenchyme.

While there was no hereditary tendency in the case reported here, the presence of such a tendency was demonstrated particularly by Preiser and Davenport. They showed that there is also a family resemblance in the location of the tumors and in other expressions of the disease such as the distribution of the cutaneous pigmentation.

In a certain number of cases mental deficiency appears. This feature was absent in the case reported here.

#### SUMMARY

A case of neurofibromatosis is reported in which there were, in addition to the typical nerve tumors cutaneous pigmentation and elephantiasis more infrequent characteristics of kyphoscoliosis with compression myelitis and sarcomatous degeneration in more than one neurofibroma.

The changes of the bones in cases of neurofibromatosis are described, and their more important features are pointed out.

The relationship of spinal deformity to compression myelitis is discussed.

## COMMENT

To the orthopedic surgeon the osseous changes in cases of neurofibromatosis are of particular interest. As the disease is considered a congenital disturbance of development other congenital skeletal deformities may be coincidental. It is therefore not surprising that reports of spina bifida, anomalies of the ribs, defects of the fibula and exostoses of various bones are associated with Recklinghausen's disease. They, however, merely exist with, and do not form a characteristic part of the skeletal picture in this condition. Of more importance are those alterations of bone which are incidental to the pathologic processes involved. They show certain typical clinical and roentgen features which help to complete the picture of the condition. Brooks and Lehman<sup>1</sup> described these changes which can be grouped under the following four headings: (1) partial atrophy and arrest of growth, (2) local hypertrophy and hyperplasia, (3) local change of pressure due to the growth of adjacent tumors and (4) unexplained osteoporosis or malacia of the long bones and the vertebral column.

The skull and the bones of the face at times participate in the pathologic processes. Palpable defects of the cranium, over which plexiform neuromas or elephantiasis of the skin is present, were described by Kienbock and Rosler.<sup>2</sup> Thinning of the cranial vault, atrophy and aplasia of the mandible, maxilla and zygoma and involvement of the squamous portion of the temporal bone and of the mastoid process may be apparent on roentgen examination. Less often the changes are those of hyperplasia and hypertrophy due probably, to an irritative effect of the overlying neuromas. The combinations of atrophy and hypertrophy may lead to various asymmetrical distortions of the head and face.

In the long bones similar changes are occasionally found. When invasion of the bone by periosteal neurofibroma occurs, softening and deformity may result. When such changes are localized the picture of defects of the bone covered with a thin layer of periosteum can be demonstrated in the roentgenogram. These are the subperiosteal cysts described by Brooks and Lehman.<sup>1</sup> When stimulation is present, areas of hyperostosis are visible. The general outlines of the shafts of the long bones are irregular. With osteoporosis pathologic fractures may follow, some of which end with pseudarthrosis. Deformities, such as coxa vara, have been reported. Fliegel<sup>3</sup> inferred that neurofibromatosis

1 Brooks, B., and Lehman, E. P. The Bone Changes in Recklinghausen's Neurofibromatosis, *Surg., Gynec. & Obst.* **38** 587 (May) 1924.

2 Kienbock, R., and Rosler, H. Neurofibromatose. Eine Neurography, *Fortschr. a. d. geb. d. Röntgenstrahlen*, supp. 42 1932.

3 Fliegel, O. Knochenveränderungen bei Neurofibromatose. *Deutsche Ztschr. f. Chir.* **193** 359, 1925.

into this cutaneous sheath an osteoperiosteal wedge for support, he intended later to break the bone graft so as to adjust it at an angle most favorable for functional purposes. He was prevented from attaining his objective because an amputation was performed by another surgeon. However, Nicoladoni's idea was adopted by other surgeons, and the operation has been repeatedly performed with good results (Nosske, Ritr and Neigesisser).

In 1897 Nicoladoni, not having lost his interest in these problems, suggested the brilliant idea of using toes to restore fingers, the operation being performed in two stages. A year later to replace a maimed thumb he transplanted the second toe from the foot on the same side. In this case Nicoladoni met with partial failure, the distal phalanx of the transplanted toe became necrotic, and active motion in the first interphalangeal joint was not possible.

The clever idea of transplanting toes drew the attention of surgeons, and the operation has probably been performed often, however, so far only seventeen cases in which good results were attained have been reported. Fifteen of the operations were performed in other countries by Nicoladoni (1898), Eisesberg (1900), Kraft (1904 and 1905), Krause (1906), Klemm (1917), Norhammer (1915), Muhsam (1917), Payer (1917), Esser (1917), Riedel (1917), Oehlecker (1917 and 1919), Gregoire (1921) and Porzelt (1924). Two cases were reported in the Soviet Union by Professor Sviatukhin (1926) and Professor Wreden (1930). Consequently my case is the third to be recorded in the Soviet Union. This comparatively small number of successful transplantations is due to a certain complexity of the operation consisting in a number of technical details, each of which plays an important part if good results are to be achieved. Therefore a detailed description of every case in which success was attained is highly instructive in indicating how technical difficulties may be overcome. Of course, the description of failures with a detailed account of the causes is no less instructive but unfortunately such cases are reported but rarely.

#### REPORT OF CASE

The patient, a girl aged 17, had received an injury of the left wrist while tobogganing. The accident was due to a breach of sporting rules, in the first place, the girl came down the toboggan-chute holding on to the edge of the sleigh, and in the second place, she and her companions started on their descent before the sleigh that had come down before them had been moved out of their way. The collision of the sleighs resulted in the girl's left index finger being completely wrenched away at the base of the middle phalanx and in a compound fracture of the middle phalanx of the middle finger.

The patient applied to the Institute in July 1933, complaining of an irregularly healed fracture of the middle phalanx of the middle finger and the deformity

osteoporosis may result from invasion by periosteal neurofibroma, the process is too generalized to make this explanation entirely acceptable. It may be supposed that the high grade of porosis with the coexisting muscular weakness can account for the severe degree of deformity. That none of these assumptions make fully understandable the peculiar and rather constant pattern of the curvature must be admitted. The supposition that the vertebral bodies partake of a more generalized congenital mesoblastic disturbance is worth considering. In other words this may be one manifestation of a generalized congenital disturbance of which the neurofibromatosis is the most constant feature. Gorlitz's<sup>6</sup> case, in which there was rather severe deformity of the spine and the thoracic cage, would suggest such an explanation.

In addition to the kyphoscoliosis all the osseous changes previously mentioned may be found in the vertebral bodies and arches. Erosion of these structures due to pressure effects from the growth of spinal neurofibroma, widening of the intervertebral foramina, local condensation and formation of cysts has been recorded.

Of unusual interest in the case reported here was the complete loss of motor and sensory control of the lower extremities associated with loss of control of the bladder and the bowels. This is perhaps the most unusual complication of Recklinghausen's disease. Rarely has complete transverse myelitis with flaccid paralysis and anesthesia been reported in a case of this disease. One such case in the French literature<sup>7</sup> and one in the German, the case of Gorlitz,<sup>6</sup> have been recorded. Several factors indicated that the lesion was one of true compression myelitis directly due to the spinal deformity. The absence of real pain especially radicular, the rapid development of the neurologic manifestations and the extreme deformity at the apex of the kyphos with correspondence of the site of involvement of the cord to this level indicated strongly that the pathologic process within the spinal canal consisted of compression of the cord by the kinked vertebral column. Injury to the cord by hour-glass neurofibromas in the intervertebral foramina can be readily ruled out, as the development of the paralysis would have been much slower, and a unilateral lesion would have been expected first. Lesions of the cord of various degrees have been reported in cases of neurofibromatosis as the result of concomitant Pott's disease, spina bifida, or other anomalies of the vertebral column, but no such changes were found in my case.

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<sup>6</sup> Gorlitz, Victor. Severe Neurofibromatosis Recklinghausen with Skeletal Deformities, *Arch f Dermat u Syph* **159** 510, 1930.

<sup>7</sup> Euziere, Lamarque, Viallofont and Longon-Turot. A Case of Recklinghausen's Disease with Kyphoscoliosis and Paraplegia, *Arch Soc d sc med et biol de Montpellier* **10** 340 (July) 1929.

of cotton between the base of the bridge and the bandage. Only after a month had elapsed and the compression of the plantar bridge no longer affected circulation in the donor (the toe) did I attempt the second stage of the operation, i. e., the cutting away of the bridge and the suturing of the tendons of the flexor. Within the next two days the recipient (the finger) was kept warm by irradiation with an infra-red lamp through the bandage.



Fig 2—Photographs of the patient taken from each side, showing the adjustment of the cast during transplantation

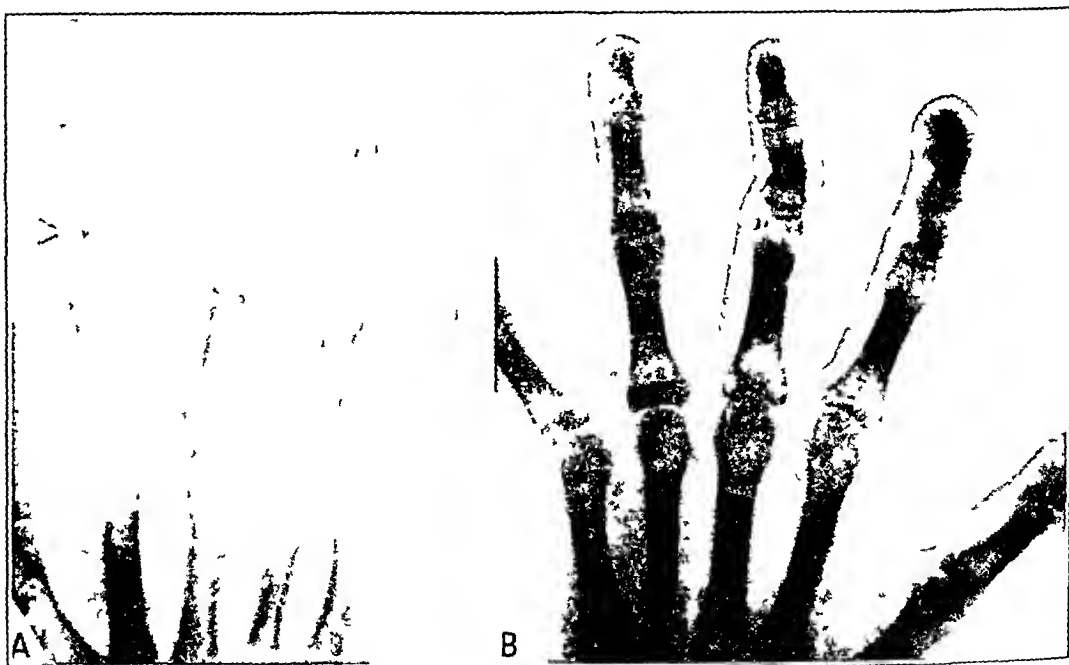


Fig 3—Roentgenograms showing the fracture of the middle phalanx of the middle finger (A) and healing after placing a wedge of bone between the phalangeal ends (B)

Seven days after the operation the sutures were removed, and the patient was treated by means of baths, massage, gymnastics and iontophoresis with potassium iodide in the outpatient department of the Institute.

Three months later the patient entered the Institute again for the correction of the badly healed fracture of the middle phalanx of the middle finger. Under

extensively involved but neurofibromas of perhaps all the cranial, spinal and sympathetic nerves have been described. In their order of frequency, changes have been noticed in the ulnar, radial, orbital, gluteal, sciatic and crural nerves according to Preiser and Davenport.<sup>11</sup> Pain is usually absent. If present it is neuralgic or neuritic. The nerves may be tender on pressure. Paralysis or atrophy rarely occurs.

The question of malignant degeneration of these tumors was fully studied by Hosoi.<sup>12</sup> He was able to collect reports of sixty-five cases from the literature. Of these metastases occurred in fourteen cases, or 22 per cent, the lungs being most frequently invaded. In 72 per cent of these cases the condition developed after the third decade of life. Rarely did a malignant process occur primarily in more than one tumor nodule. The case reported here is therefore of additional interest in that malignant degeneration of various degrees was present in almost all the larger tumors studied (seven). Except for the advanced changes in the extremely large tumor all the others were of similar appearance macroscopically and microscopically. Malignant degeneration had reached an equal stage in all. As no other structures were involved in the malignant process, one must suppose that on the basis of previously benign lesions sarcomatous degeneration took place simultaneously in several neurofibromas rather than that the changes were metastatic. The transition from a benign to a malignant process seems to have coincided with the period of rapid growth of the large tumor. This rapidity of growth was evident histologically from the sharp division between the living and the dead tissue without a necrobiotic zone and from the presence of structural outline where necrosis existed, indicating the inability of the blood supply to keep pace with the accelerated anaplasia. When the growth of a benign tumor undergoes unusual stimulation, the presence of malignant changes must be strongly suspected.

The typical coffee-colored spots and areas of elephantiasis have been too frequently described to necessitate further discussion. That these changes are dependent on a pathologic process in the subjacent nerves is a reasonable assumption in view of the widespread involvement of the peripheral nerves. Eller<sup>13</sup> reported several cases in which the typical cutaneous changes were present without any palpable neurofibromas having been found. However, as later observations revealed the

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11 Preiser, Samuel A., and Davenport, Charles B. Multiple Neurofibromatosis (von Recklinghausen's Disease) and Its Inheritance, *Am J M Sc* **156** 507 (Oct) 1918.

12 Hosoi, K. Multiple Fibromatosis with Special Reference to Malignant Transformation, *Arch Surg* **22** 258 (Feb) 1931.

13 Eller, J. J. Incomplete Form of von Recklinghausen's Disease, *Arch Dermat & Syph* **17** 648 (May) 1928.



of the grasp and the pressure exerted by the thumb and the grafted index finger were no less than those of the other hand. The patient was much pleased with the results of the operation, the symptoms of mental depression had completely disappeared as soon as the defect of the finger was repaired, and the patient, who previous to the operation was always hiding her maimed hand, now readily submitted it to examination.

The foot with the amputated toe caused the patient no unpleasantness. Even in cases in which the thumb has to be replaced I believe it more rational to use the second instead of the great toe, both for cosmetic considerations and for preservation of the statico-dynamic function of the foot, in which the great toe is of the utmost importance. This statement is confirmed by the results in one of Oehlecker's cases in which the function of the foot was found to be disturbed subsequent to the grafting of the great toe.

On the ground of the aforementioned data the results in this case should be considered entirely successful, a fact which has been fully acknowledged at the meetings of the two surgical societies at which the patient was presented. By no means all of the eighteen reported cases of successful grafting of toes (the present case included) may be regarded as entirely satisfactory from the functional point of view. In ten of the eighteen cases the function of the recipient was barely satisfactory, in four cases (those of Klemm, Esser, Norhammer and Oehlecker) the function was good, and in the four remaining cases (those of Riedel, Sviatukhin and Wieden and mine) the fingers completely fulfilled their normal function and proved to be genuine substitutes for the lost members. Thus in performing the operation the surgeon has to cope with two tasks of increasing complexity. The first consists in insuring the healing of the grafted toe, and in my opinion the success of this part of the operation is chiefly determined by allowing the necessary time to elapse before the second stage, the separation of the bridge, is attempted, the second task is more complicated, for it consists in insuring active motor function in the finger, which makes it necessary to overcome certain technical difficulties.

In Prof. R. R. Wreden's clinic so far only two attempts to perform the operation have been made (those by Wreden, 1930 and me, 1933), both operations proved successful. I believe that the good results in my case should be attributed to the fact that a number of technical details were carefully worked out and it is the chief object of this paper to present a full account of these details.

1. The pedicle should be made on the side of the sole, for the plantar arteries are better developed than the dorsal, and they therefore insure a better blood supply. Besides it saves the patient a great

# TRANSPLANTATION OF A TOE ACCORDING TO THE METHOD OF NICOLADONI

REPORT OF A CASE

PROF M I KUSLIK

LENINGRAD, U S S R

The branch of surgery which is known by the name of 'restorative surgery' and which aims at reestablishing lost functions and correcting cosmetic defects is one of the most fascinating. The possibility of restoring to the maimed their capacity for work and of freeing them from the mental depression caused by the realization of their infirmities is one of the noblest works a surgeon can perform. It brings him satisfaction and restores balance to the patient's life. Because of this, many of the most gifted surgeons have long since directed their efforts toward restorative surgery, which has achieved particularly great development within the last decade largely in connection with the theoretical and practical study of plastic procedures. The healing on of parts of extremities which have been lost in the accomplishment of which primary reimplantation and secondary grafting are distinguished as different methods is of particular interest.

The healing on of completely severed finger-tips should be considered as the first experiment made within this particular field of surgery. Hopfner's experiments which resulted in partial adhesion of an amputated extremity in a dog served to show that it was possible to attempt reimplantation of even larger sections of the extremities. J. J. Moore succeeded in reimplanting the forearm in man, and three years after the operation he had occasion to observe that the sensory, motor and vasomotor disturbances were considerably decreased. However, the success of similar operations demands a number of favorable conditions and therefore the practical importance of reimplanting extremities is by no means great. Such cases as these will always be rare. On the other hand, secondary grafting which aims at compensating for the defects of such functionally important working levers as fingers seems to offer much greater possibilities.

The initiator of plastic surgical treatment of tendons, Nicoladoni, was also the first to make a new attempt in the second field of surgery. As early as 1891 he attempted to restore part of a thumb by means of a skin graft taken from the chest, with the intention of inserting

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seven days enough. Other authors have suggested intervals of varying duration within the range of the two just mentioned.

I believe that an interval can hardly be determined which will apply to all cases, as it depends on the establishment of nutrition in the pedicle. This is determined by the reaction shown in its circulation after compression of the pedicle. It is obvious that in different cases the interval will be of different length, it may depend on the patient's age, on his general condition, on the size of the graft and other factors.

6. Within the first days after the operation I believe it highly advisable to keep the recipient warm by means of an electric bath, infra-red lamps, etc.

The strict observance of the technical suggestions just made will to a great extent insure the success of the operation. The patient's invalidism lasts from one and one-half to three months.

Taking into consideration the moral and economic effect of the procedure, I propose that it be more widely applied in the future, for the operation should no longer be regarded as a surgical experiment. It has become a well grounded and effective method of restoring ability to work and of overcoming cosmetic defects.

of the index finger, which was the cause of constant depression. Within the same month the patient was subjected to the first stage of the operation performed according to Nicoladoni's method. Local anesthesia was employed. The distal surface of the stump of the finger was cut open by means of an arched incision, the tendon of the extensor muscle isolated, the surface of the phalanx exposed and the periosteum separated around it to a depth of about 0.5 cm. Furthermore, an incision forming a cutaneous flap was made at the base of the second toe of the left foot on the dorsal surface, both the dorsal interosseous arteries having been divided. The tendon of the extensor muscle of the toe was cut as far proximally as possible (fig. 1). One centimeter distal to the proposed level of division of the bone the periosteum was separated and turned back as a

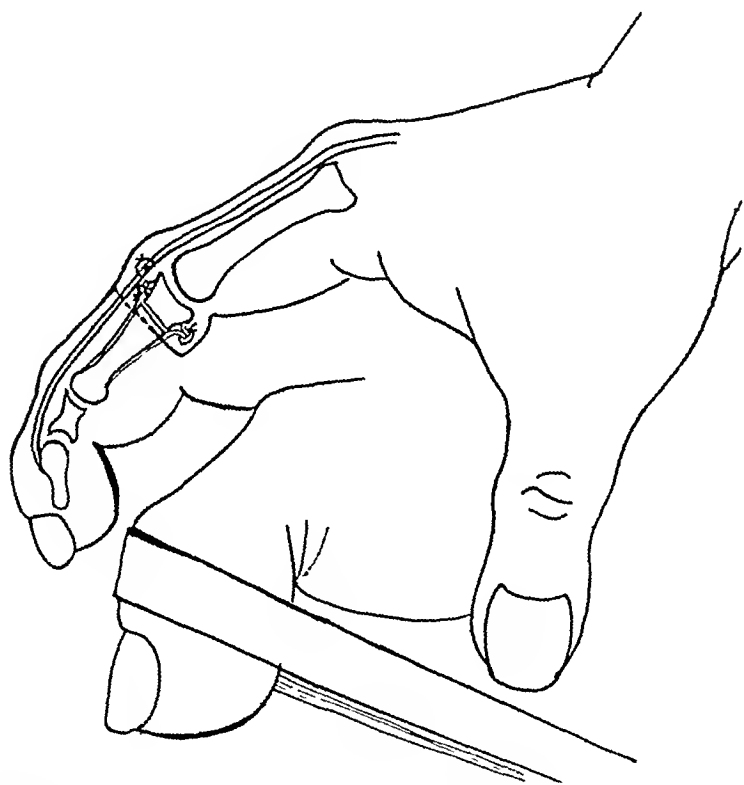


Fig. 1—Drawing showing the first stage of transplantation of a toe on the index finger.

cuff, after which the bone was divided. The distal end of the phalanx of the toe was dislocated in the wound and adjusted exactly opposite the newly sectioned phalanx of the stump of the finger. The edges of the previously separated periosteum were fastened together by means of a circular suture of catgut with the object of strengthening the contact between the fragments of bone. The sutures binding together the ends of the tendons of the extensors were made somewhat proximal to those securing the periosteal edges, while suture of the skin was passed so as not to coincide with the level of that of the tendon. Finally, the patient having been placed in a sitting posture, a plaster of paris dressing was applied reaching to the upper edge of the shoulder blades (fig. 2).

In ten days an opening was cut in the plaster of paris bandage, and the regular pressing down of the plantar bridge was begun by inserting a tightly rolled ball

termination of the second or accessory cystic duct may be in the common duct or in one of the hepatic ducts. Of 22 cases in which the exact terminations of the cystic ducts were demonstrated, the "Y" type of duct was present in 7 (fig 1*A*) and a "ductular" variety, or two completely separated ducts (fig 1*B*), in 5

An accessory gallbladder may be adjacent to the normal organ and thus lie in the normal fossa of the gallbladder (fig 1*A*, *B* and *C*). When the two gallbladders lie next to one another they are often invested with a common peritoneal coat, and the true duplicate nature of the organ is therefore occasionally overlooked at the operating table. More

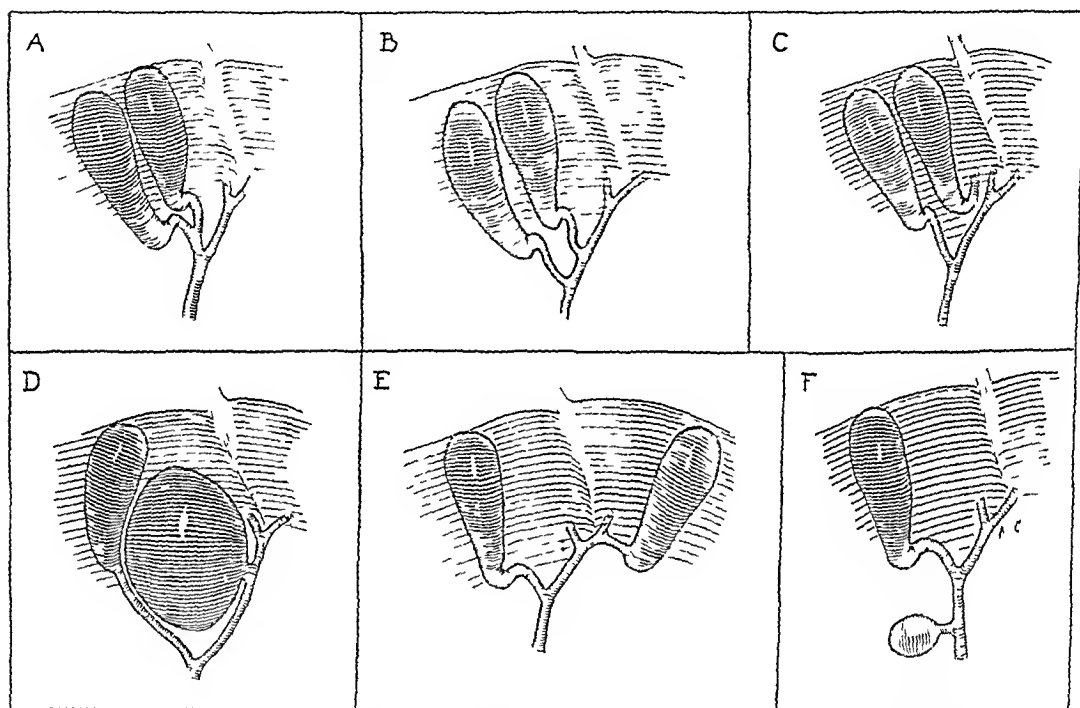


Fig 1—Types of double gallbladder, showing the positions of the accessory organs and the distribution of their ducts. *A* shows the gallbladder in the normal fossa with Y-shaped cystic ducts, *B*, in the normal fossa with two separate cystic ducts, and *C*, in the normal fossa with an accessory cystic duct directly entering the hepatic substance. *D* shows an accessory gallbladder partially embedded within the right lobe of the liver and communicating with the main hepatic duct, *E*, an accessory gallbladder under the left lobe of the liver and communicating with the left hepatic duct, and *F*, an accessory gallbladder in the gastrohepatic ligament and communicating with the common duct.

often there is a fissure between the two gallbladders, or else they are not covered by a common coat and the double structure is evident. The accessory gallbladder may lie in positions other than in the normal fossa. It may be situated under the left lobe of the liver and may communicate

local anesthesia the bone was refractured. The distal end of the phalanx was then correctly adjusted, and a small wedge taken from the same phalanx was placed between the fragments so as to keep them in place (fig 3).















Five months after the first operation the patient was presented before the Leningrad Society of Orthopedic Surgeons and the Pirogoff Surgical Society. Both the functional and the cosmetic results were found to be highly satisfactory (fig 4). The line of grafting was manifest only by a narrow scar which was barely visible. The mental state of the patient was greatly improved.



Fig 4—Photographs showing good results of the operation on the index and middle fingers five months after the first operation.

In the case reported by Klemm sensation was not completely restored until the end of the second year after the operation. This may probably be accounted for by the fact that the scar along the line of grafting was somewhat thicker because healing occurred by second intention. My patient could use her finger to its full functional capacity, and it is of interest to note that the skin on the finger-tip had become somewhat callous, this was probably due to the fact that the skin of the toes is less adapted to work than that of the fingers. The strength

TABLE 1—Data in Cases of Double Gallbladder

Case	Author	Year	Sex	Age, yrs	Symptoms	Physical Findings	Röntgen Findings	Pathologic Observations	Type of anomaly
1	Sherren	1911	F	25	Attacks of pain in right upper quadrant after meals for many years	Tenderness in area of gallbladder		Symptoms from aberrant Brunner's glands in cystic duct terminations of duets?	
2	Schulz	1914	M	35				Y shaped cystic duets, terminating in common duet stones in both gallbladders	
3	Schaefer	1916	F	52	Gallstone colic for from 15 to 20 years			Fissure between gallbladders terminations of cystic duets unknown, stones in gallbladders	
4	Haberer	1923	F		Severe gallstone colic	Gallbladder palpable		Falts of cystic duet unknown stones in both bladders	
5	Wischnewsky	1925	F	31	Fever, jaundice and weakness	Palpable tense gallbladder		Accessory gallbladder under left lobe of liver terminations of cystic duets (?)	
6	Braun	1926						Cystic duets with separate openings into biliary tree, one gallbladder half size	
7	Erdman	1926						Y shaped cystic duets terminating in common duet	
8	Hardesty	1926						2 cystic duets, joined before entering common duet	
9	Lambert	1926						Cystic duets emptied separately into common duet	
10	Nichols	1926	M	51	Attacks of jaundice and pain in right upper quadrant and alcoholic stools for 10 yrs	Tenderness in gall bladder area	2 rows of gall stones	Terminations of cystic duets not stated stones in both gall bladders	
11	Niehols	1926						Falts of cystic duets not determined	
12	Garafola	1927	F	37	Colicky pain in right upper quadrant, nausea and vomiting for 5 yrs	Small mass in region of gallbladder		One gallbladder half size of other stones Y shaped cystic duets (?)	
13	Priesel	1927	M	54	No symptoms from biliary tract (died of appendicitis)			Cystic artery behind both duets and then in fissure between gallbladders	
14	Wakeley	1927	M	56	Attacks of abdominal pain radiating to right shoulder and jaundice for 6 yrs	Tenderness in right side of hypochondrium	Stones in 1 gall bladder	Y shaped cystic duet stones and inflammation of one gallbladder other normal	

deal of inconvenience to have the wrist placed on the dorsal surface of the foot with the fingers encircling it rather than fixed under the sole of the foot, the more so that in the latter case the hip and knee have to be brought into a position of still further flexion, which is especially hard to bear. Hence in performing the first stage of the operation I leave a plantar bridge with two plantar arteries.

2 It is of great importance as far as the functional success of the operation is concerned that the level of the osseous tendinous and cutaneous sutures should not coincide. When the case of the patient whom I presented was under discussion, Prof. J. J. Jenalidze suggested that, contrary to Bunnell's method, only the deep-lying flexor of the recipient should be sutured in the second stage of the operation, the superficial flexor being ignored, with a view to simplifying the technic.

3 To insure a better contact and fixation of the osseous fragments, suturing of the periosteal cuffs made previous to the osteotomy of the phalanx of the toe and freshening of the wound of the phalanx of the stump of the finger are advised.

With a view to obtaining a better contact between the ends of the phalanges Professor Sviatukhin advised in the first stage the resection of the superfluous central portion of the phalanx and the head of the corresponding metatarsal bone.

Fully appreciating the importance of the suggestion, I object to the resection of the head, for on this depends to a great extent the function of the foot.

4 Many of the patients find it extremely hard to endure the highly inconvenient position in which they are forced to remain for a considerable period of time. Their constant complaints have not infrequently led surgeons to attempt the second stage of the operation somewhat prematurely, a fact to which a number of failures may be attributed. With a view to alleviating these painful conditions I apply a plaster of paris bandage (fig. 2) which encases the upper and lower extremities on the side of the operation as well as the body at the back reaching to the upper edge of the shoulder blades. In such a bandage the patient seems to sit leaning on the back of an armchair. The difficult problem of sleep is simply solved, the patient is put to bed lying on his side. A great deal may be gained by training the patient to maintain the necessary position prior to the operation.

5 Various authors have recommended different intervals between the first and second stages, the length of time varying considerably. For instance, Porzelt performed the second operation on the thirty-third day after the first, while Sviatukhin considered an interval of



from the normal cystic duct would produce a double structure with a Y-shaped cystic duct

In contrast to those accessory gallbladders which arise from the extrahepatic ductular system there is a second form which has been designated the trabecular gallbladder (Boyden) because it arises from the hepatic trabeculae bordering the fossa vesicae felleae. Such a gallbladder always lies adjacent to the normal one, but its duct turns and courses directly into the substance of the liver. Such an anomalous structure probably represents an outpouching from the liver cell cords, and as such it develops a communication with the smaller bile capillaries. Boyden observed 4 of these accessory trabecular gallbladders in his series of calves and 1 in a sheep. The only example ever recorded in man is that published by Croudace (fig 1C, table 1, case 22).

The reports of these cases do not give any characteristic symptoms or signs which might be of aid in diagnosing the presence of the congenital anomaly before operation or autopsy. When the accessory organ is the seat of inflammatory change or stone formation, the symptoms and signs are indistinguishable from those occurring with cholecystitis or cholelithiasis in a normally formed gallbladder. The mere presence of a second vesicle has not clearly given rise to symptoms in any case. Whether or not an accessory organ is more prone to be involved by disease processes is difficult to state, but the fact that most of these anomalies have been found at the operating table and only a few at postmortem examinations tends to show that the accessory structure is probably more likely to have pathologic changes than is a normally formed organ.

Roentgenographic examination has demonstrated a duplicate gallbladder in 5 instances. Climan in 1929 reported a case in which there was a second shadow which lay behind and below the first gallbladder shadow. Ten minutes after the ingestion of a fatty meal both shadows were reduced in size, and evidence of a distinct double gallbladder was more pronounced. Both vesicles showed good concentration of the dye and normal reduction in size after the fatty meal was taken. In Nichols' first case (1926) there were two distinct rows of stones in the region of the gallbladder which could not be approximated by manipulation of the gallbladder (fig 2). In 1931 Hayes demonstrated two dye shadows indicative of a double organ (fig 3). Cave (in 1931) recorded 2 additional examples of double gallbladders detected by cholecystography. In each of the last 2 cases, one gallbladder concentrated the dye and emptied normally while the contiguous gallbladder failed to empty properly.

A report of a case of double gallbladder follows.

G. B., aged 3 years and 3 months, entered the Children's Hospital in August 1932 because of a chronic infection of the respiratory tract of two and one-half

# CONGENITAL ANOMALIES OF THE GALLBLADDER

A REVIEW OF ONE HUNDRED AND FORTY-EIGHT CASES, WITH  
REPORT OF A DOUBLE GALLBLADDER

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BOSTON

Congenital anomalies of the gallbladder are rare, but it is desirable for the roentgenologist and surgeon to be familiar with the malformations of this organ which they so commonly examine and operate on. Malformations of the bile ducts and their associated blood vessels have been admirably emphasized by Eisendrath, Haberland, Holmes, Howard and Wolbach, Kehr, Ladd, Mentzer and others, but such treatises have not included any comprehensive study of the gallbladder. It is my purpose in this presentation to collect from the literature the isolated reports relevant to the subject of anomalies of the gallbladder and to present this material in a unified manner. The review has been extensive but not exhaustive, for many articles have appeared in periodicals that were not available, and other examples have doubtless been overlooked. Numerous cases of the types under discussion were recorded before 1900, and while many of these were well described, only the more recent reports are employed. A study of the following 148 cases is adequate to illustrate the different types of abnormalities of the gallbladder. Histologic studies have usually been lacking, and the descriptions have been more concerned with gross findings. Notes on the vascular systems about these gallbladders are very poor, and in order that the course and distribution of the associated blood vessels may be better understood, future examinations and reports should include such data. Boyden's anatomic studies on the accessory gallbladder have been freely used in the preparation of the following sections.

## ANOMALOUS FORMS OF THE GALLBLADDER

*Double Gallbladder*.—The term "double gallbladder" has been employed to describe 28 examples of reduplication of the vesica fellea in each of which there were two separate gallbladder cavities and two separate cystic ducts. The two cystic ducts may subsequently converge and form a joint cystic duct which enters the ductus choledochus (Y-shaped type), or the two cystic ducts may empty separately into the extrahepatic biliary system (ductular type). In the latter form the

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months' duration. He died two days after entry to the hospital. At no time during the patient's life had there been any symptoms referable to the biliary tract.

Autopsy showed acute and chronic bronchopneumonia, bronchiectasis and fibrinopurulent and fibrous pleuritis. The observations of particular interest were limited to the liver and the biliary system. The liver weighed 500 Gm and showed no evidence of cirrhosis or of biliary stasis. The under-portion of the liver was

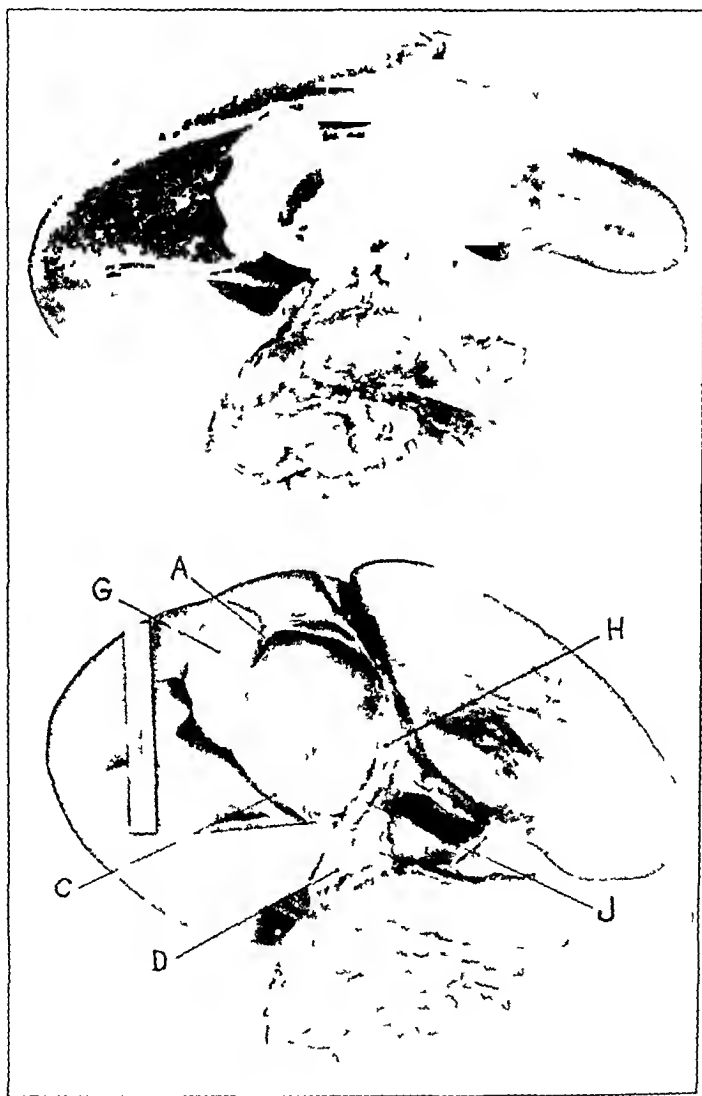


Fig. 4—Photographs of the liver and double gallbladder in the case here reported. The accessory gallbladder is spherical and extends far up into the substance of the right lobe of the liver. *A* indicates the accessory gallbladder, *C*, the normal cystic duct, *D*, the common duct, *G*, the normal gallbladder, *H*, the hepatic duct, and *J*, the junction of the accessory gallbladder to the hepatic duct.

abnormal because of the presence of a large hemispherical cavity within the substance of the right lobe. The cavity was open below and extended up into the







with the left hepatic duct (fig 1E) Another location is demonstrated in the case reported at the end of this section, in which the accessory organ was largely embedded within the right lobe of the liver and communicated with the main hepatic duct (fig 1D) A fourth location is on the under-surface of the liver or within the gastro-hepatic ligament, the accessory organ having a communication with the common duct (fig 1F)

The size of an accessory gallbladder is usually approximately the same as the normal structure, but occasionally it is only a half or two thirds of these dimensions The anomalous gallbladders which arise from the common duct and lie along the gastrohepatic ligament are uniformly small and rudimentary structures which are from 1 to 2 cm in overall length The accessory gallbladder described here (fig 1D and fig 4) was much larger than the primary vesicle In 23 cases for which such data are recorded, 17 duplicate vesicles occurred in females and 6 in males Sixty-four per cent of these cases were discovered in the age groups between 30 and 60 years, the youngest person was 14 months of age, and the oldest, 69 years

Boyden in 1926 collected and analyzed cases of accessory gallbladder in man and in animals In the section on double gallbladder in human beings he listed 6 cases from the older literature which have not been included here He also mentioned a specimen from the Hamann Museum for which few anatomic data were given In a thorough study of animal material Boyden found 23 examples of double gallbladder in 2,600 cats, 47 cases in 2,555 calves and 3 cases in 2,560 lambs and sheep

The embryologic explanation of the formation of these double vesicles varies somewhat with the form of the duplicate structure A secondary gallbladder connecting with the cystic, hepatic or common duct probably arises from the small outpocketings which are so frequently seen on these ducts in embryonic life and which apparently represent a normal stage in the development of the extrahepatic biliary system Such rudimentary and additional duct buds are common in human embryos and may spring from any one of the primary ducts, but they are most common at the junction of all three ducts (Keibel and Mall) Boyden found (in vertebrate embryos) a hepatic antrum at the junction of the cystic, hepatic and common ducts and showed that from this dilated portion of the ductal system there are numerous outgrowths and accessory vesicle formations These supernumerary buds normally regress but the persistence of one of them would doubtless result in formation of an accessory gallbladder A second accessory gallbladder thus originating on the hepatic or common duct would be of the ductular variety, for it would connect with the biliary tree separately from the normal cystic duct A second gallbladder arising

TABLE 2—Data in Cases of Bilobed Gallbladder

No of Case	Author	Year	Sex	Age, Yrs	Symptoms	Physical Findings	Roentgen Findings	Pathologic Observations	Type of Anomaly
1	Deaver and Ashurst	1914	F	55	No symptoms referable to biliary tract (death from apoplexy)			2 lobes of unequal size, calculus in larger one, other one normal	
2	Ryeroft	1923	F	42	Attacks of biliary colic with jaundice for 13 yrs	Tenderness in right side of hypochondrium		Gallbladder divided into 2 cavities by long septum, 1 calculus present	
3	Ullmann	1926					Seen by chole cystography	V shaped structure, lobes separated at fundle portions	
4	Meyer	1926	F	55	Gallstone colic, fever and jaundice			2 separate but approximated lobes covered by a common peritoneal coat	
5	Phillips, Isaacs and Macdonald	1931	M	48	(Recurrent pancreatitis and icterus)	Tenderness in left flank, jaundice		V shaped structure marked inequality in size of lobes	
6	Phillips, Isaacs and Macdonald	1931	F	56	Recurrent attacks of biliary colic for 2 yrs			Gallbladder cavity partitioned by central fibromuscular septum	

1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.
1	Climan	1929	I	27	Epigastric pain following meals for 5 yrs	Tenderness in right upper quadrant	Dye seen in 2 gallbladders	2 gallbladders functioned normally by cholecystography, no operation						
16	Judd, McIndoe and Marshall													
17	Wolfson	1929	I	19	Attacks of pain in right hypochondrium, with vomiting for 9 yrs	Slight tenderness in right upper quadrant	Single group of stones	Accessory bladder 1.5 cm long, with stones and unattached to liver						
18	Holderman	1930	F	30	Attacks of pain in right upper quadrant chills and vomiting for 7 yrs	Rigidity in right upper quadrant	Not visualized	Gallbladders adjacent to each other openings of cystic ducts not stated						
19	Petrina	1930	I		Epigastric pain			2 separated cystic ducts						
20	Cave	1931	I	40	Vague abdominal symptoms suggestive of pathologic condition in gallbladder		2 shadows of dye seen	Inner vesicle functioned poorly no operation						
21	Cave	1931	I	40	Symptoms suggestive of gall bladder disease		2 shadows of dye seen	Outer vesicle functioned poorly no operation						
22	Croudaec	1931	F	52	Colicky pain of biliary type for 2 days dyspepsia for several years	Marked tenderness in area of gall bladder	1 shadow seen	Accessory organ half size with stone, accessory cystic duct led into liver						
23	Hayes	1931	M	35	Indefinite gastro intestinal symptoms		2 dye shadows seen	2 gallbladder shadows demonstrated by roentgenogram no operation						
24	Strukow	1931	M	1	No symptoms referable to biliary tract (died of scarlet fever)			Incidental autopsy observations 2 separate cystic ducts, opening into common duct						
25	Hermann, Hicks and Martin	1933	I	42	Epigastric pain radiating to back, nausea, jaundice and pruritus	Icterus tenderness in right side of hypochondrium		Muscularis and mucosa in each gallbladder, stones in common duct and both gallbladders						
26	Kennon	1933	M	60				5 in long gallbladder with stones 3 in gallbladder without stones separate ducts						
27	Slaughter and Trout	1933	I	32	Attacks of pain in right upper quadrant, vomiting for 2 yrs	Tenderness below right costal margin	Not visualized	Accessory gallbladder 5 cm long, partly buried in liver, Y shaped cystic duct						
28	Gross	1936	F	3	No symptoms referable to biliary tract (died of bronchopneumonia)		No roentgenogram made	Accessory gallbladder 7 cm in diameter, partly buried in liver, opening to hepatic duct						

TABLE 3—Data in Cases of Diverticulum of the Gallbladder










No of Case	Author	Year	Sex	Age, Yrs	Symptoms	Physical Findings	Roentgen Findings	Pathologic Observations	Type of Anomaly
1	Kamerer	1912	F	48	Symptoms of a well marked recurring cholecystitis			Diverticulum $1\frac{1}{2}$ in diameter in region of cystic duct	
2	Nadeau	1917	F	29	Pain in lower quadrant and epigastric pain for 3 mos	Tenderness in right lower quadrant		Large diverticulum projecting into liver and showing on anterior surface of liver	
3	Elsendrath	1918						Diverticulum of body of gallbladder with stones; cystic ducts passing into liver	
4	Abbott	1923	F	35	Attacks of pain in right side of hypochondrium and in back for 2 yrs	Negative		Diverticulum $1\frac{1}{2}$ in long at neck of gallbladder	
5	Barsony	1927	F?				Seen in roentgenogram	Diverticulum of body of gallbladder no operation	
6	Barsony	1927					Detected in roentgenogram	Hazel nut sized diverticulum at fundus, no stones or inflammatory reaction	
7	Barsony and Fredrick	1928	F	23	Attacks of abdominal pain radiating to back with vomiting for 7 yrs	Palpable gall bladder	Seen by cholecystography	Diverticulum of body of gallbladder	
8	Kremer	1932		38			Seen by cholecystography	Diverticulum of body of gallbladder	
9	Vastine	1934	F	38	Epigastric distress after meals	Epigastric tenderness	Stone in diverticulum	Diverticulum 1.3 cm in diameter at fundus of gallbladder	



Fig 2—Roentgenogram of a double gallbladder showing two rows of stones in the two gallbladders (Nichols' first case, reproduced from *Radiology* 6 255, 1926 )

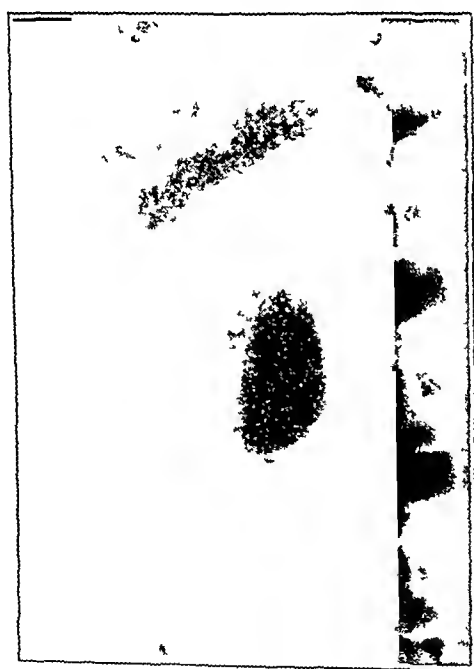


Fig 3—Roentgenogram of a double gallbladder, showing dye in two separate gallbladders. Other films showed the gallbladders spread apart (Haves' case, reproduced from *Radiology* 16 66, 1931 )



verse incomplete septum pinching off a small cavity at the tip (fig 6D) may be developed as an incomplete resolution of the solid stage through which the gallbladder passes in embryonic life. Thus a constricting band or incomplete diaphragm is left in the same manner as a congenital stenosis or atresia is developed in the small intestine.

*Absence of the Gallbladder*—Total absence of the gallbladder is represented by the 38 cases listed in table 4. Only those cases are tabulated in which the hepatic and common ducts were present and functioning and in which the absence of the gallbladder was the only abnormality. There is a larger group of cases which are not included in this review. In these, in addition to absence of the gallbladder, there was atresia of all or some portion of the hepatic or common duct system. Approximately 200 cases of atresia of the extrahepatic bile passages have been recorded in the literature, and in about one sixth of these there was absence of the gallbladder.

Agenesis of the vesica fellea may occur without any other variation from the normal in the remaining extrabiliary system, as is demonstrated by the 38 examples listed in table 4. The fossa of the gallbladder was commonly absent, but occasionally a shallow fissure or dimple was visible on the under surface of the right lobe. Numerous authors observed that the quadrate lobe was poorly defined or entirely missing. Absence of the gallbladder was twice as common in females as in males. The ages of these patients when the anomaly was discovered, at operation or autopsy, varied from a few days to 65 years, with an average of about 35 years. Twelve of the abnormalities were observed in persons between the ages of 45 and 65. As far as could be determined from the reports, the absence of the gallbladder did not in any way impair the health or digestive functions of these persons. The absence of the gallbladder, per se, was rarely accompanied by any compensatory dilatation of the hepatic or common ducts, and many authors commented on the normal size of these structures. When the extrahepatic ducts were dilated the presence of gallstones raised the possibility that the increased size was due to obstruction from calculus rather than from absence of the gallbladder.

The absence of a gallbladder may be explained in two ways. The hepatic diverticulum arises from the foregut to form the liver, the extrahepatic ducts and the gallbladder. The gallbladder and cystic duct normally originate from this diverticulum as an outpocketing, but the failure of the latter development would cause complete absence of the gallbladder and cystic duct. A second way in which absence of the gallbladder might be explained is by the failure of the gallbladder bud to resolve from its solid embryologic stage. The hepatic, common and cystic ducts, as well as the gallbladder, are hollow structures in early embryonic life but later

liver, so that only a rim of the substance of the liver from 4 to 5 mm thick remained at the dome of the right lobe. The cavity, which was about 7 cm in diameter, lay above and to the left of the normal fossa of the gallbladder and was completely filled with a spherical, thin-walled accessory gallbladder which was 7 cm in diameter (fig 4). This bladder was filled with normal bile. Leading from the left lateral and the posterior portion of this saccular structure there was a small duct 3 mm in diameter and from 4 to 5 mm in length which communicated with the midportion of the main hepatic duct.

The primary gallbladder was normal in appearance and essentially normal in size for a patient of this age. It was 4.5 cm long and 1.5 cm in its greatest diameter. Its walls showed no evidence of inflammatory change. The cystic duct was 4.5 cm in length. This elongated duct coursed around the right lateral aspect of the accessory gallbladder to enter normally at the junction of the hepatic and the common ducts. This primary gallbladder contained colorless mucous fluid which at first could not be expressed down into the common duct and the duodenum. The presence of this white bile was apparently due to pressure on the primary cystic duct by the adjacent distended accessory gallbladder, for when the latter vesicle was deflated the primary cystic duct was found to be patent.

Microscopic examination of the wall of the accessory gallbladder showed it to be composed entirely of a dense band of hyalinized connective tissue. There was no smooth musculature. The inner layer lacked an epithelial lining. There were no mucosal glands. A few small masses of inspissated bile were found on some portions of the inner surface. There was no evidence of inflammatory reaction in the wall.

*Bilobed Gallbladder*.—This anomaly, which is so common in many of the higher vertebrates, is seldom encountered in man (table 2). *Vesica fellea divisa*, as the name implies, is a gallbladder with a bifid or partially divided structure. Included in this group are those specimens which have two cavities both of which are drained by a single cystic duct.

Two types of this malformation are seen. In the first of these the gallbladder appears normal to external inspection, but when opened it is found to have a longitudinal septum dividing the organ into two chambers. These two cavities communicate at their proximal ends and are supplied by one duct (fig 5A). This septum is fibrous, but may contain a smooth musculature. Glandular elements have been described in the septal mucosa. The second form of bilobed gallbladder has a complete division of the fundic portion, with a fusion of these portions at the neck of the gallbladder. The cleft is shallow in some instances, but in other cases it almost completely divides the gallbladder into two parts. Externally such an organ has a V shape. The two cavities are thus completely separated at the distal ends but communicate with one another at the base and have a common exit through one cystic duct (fig 5B). The two arms of such a gallbladder are usually of equal size, but occasionally one branch may be smaller than the other.

TABLE 4—Data in Cases of Absence of the Gallbladder—Continued

No of Case	Author	Year	Sex	Age, yrs	Symptoms	Physical Findings	Pathologic Observations
22	Nagel	1926	M	33			No gallbladder
23	Golob	1927	F	59	Gaseous eructations and feeling of pressure in epigastrium for 1 yrs	Essentially negative	No gallbladder
24	Ishiyama	1927	F	50	Yearly attacks of jaundice and pain in right side of hypochondrium for 29 yrs	Icterus achollic stools	No gallbladder, stones in common duct, common duct "enormously dilated" and thickened
25	Lintz	1927	F	48	Pain in right upper quadrant radiating to back for 5 yrs		Gallbladder absent had a large Riedel's lobe on liver
26	Bower	1928	M	50	Severe pain right upper quadrant with jaundice	Tenderness and rigidity in right side of epigastrium	No gallbladder or cystic duct no gallbladder fossa, absence of left lobe of liver, pancreatitis
27	Schmidt	1928	F	30	Colicky epigastric pain and loss of weight for 6 mos	Liver enlarged and tender	No gallbladder or gallbladder fossa, gumma of liver
28	Brack	1929	M	22			No gallbladder
29	Meyer	1929	M	21	Colicky abdominal pain	Mild jaundice	No gallbladder
30	Machmull	1930	M	37	Died of tuberculosis		No cystic duct or gallbladder
31	Barnstorf	1931	F	19	Died by drowning		No gallbladder, common duct of normal size
32	Amadon	1933	M	51	Chronic indigestion, pain in right upper quadrant and shoulder	Epigastric tenderness	No gallbladder or cystic duct absence of quadrate lobe

have their lumens temporarily obliterated during the so-called solid phase through which all these structures pass. These lumens are all later reestablished, and the normal organs are formed, but an arrest in this obliterated stage produces atresia of any portion of the extrahepatic system (in the same manner in which intestinal atresia is derived). When there is atresia of the extrahepatic ducts or gallbladder there is usually a visible solid fibrous cord found representing ducts and gallbladder in infants who die of this condition. In contrast to these findings of a rudimentary cord in the fossa of the gallbladder in cases of associated atresia of the ducts, no such rudimentary structure was reported in any of the cases listed in table 4. The belief is therefore established that in the group of cases listed in this section the gallbladder is absent because of the failure of development of the gallbladder bud from the hepatic diverticulum.

*Miscellaneous Malformations of the Gallbladder*—There are several forms of gallbladder which deserve only passing mention. An hour-glass gallbladder is frequently described, but from most of the reports it is not clear and is indeed impossible to tell whether it is the result of inflammatory change and subsequent cicatricial contraction. There are, however, examples in which this is undoubtedly a congenital malformation, particularly those occurring in younger children in whom there is

In the cat Boyden found that this was the most common anomaly of the gallbladder. He observed it 272 times, or in 10 per cent of all the animals examined. He also recorded 30 bilobed specimens in 2,555 calves and 27 in 2,560 lambs and sheep and 5 cleft gallbladders in 2,572 pigs.

The embryologic explanations of bifid V-shaped gallbladders has been clearly demonstrated in the cat (Boyden), and the same process possibly applies to man. In the cat the embryonic gallbladder frequently acquires a paired form by a subdivision of its primordium. When this structure is in the solid stage a splitting of it in a longitudinal direction changes this single bud into a partially divided organ. These paired buds maintain a connection with each other, but the fundic ends remain separated. The bilobed gallbladder in which the two cavities are separated only by a longitudinal septum probably represents an incomplete resolution of the solid stage through which the structure of the gallbladder

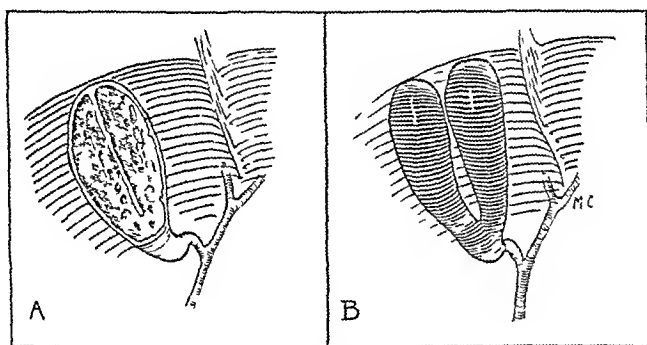


Fig 5—Forms of bilobed gallbladder having one cystic duct. A, a gallbladder with normal external contour but with two cavities separated by a septum, B, a gallbladder paired at the fundic portion and joined at the neck of the gallbladder.

normally passes. Instead of the entire cavity being again reestablished, a portion of the solid elements remains to form a fold or septum.

*Diverticulum of the Gallbladder*—A diverticulum of the gallbladder may occur anywhere along the surface of the organ from the fundus to the neck (table 3). The diverticula vary in size from  $\frac{1}{4}$  to  $1\frac{1}{2}$  inches (0.64 to 3.8 cm) in diameter. Only a small number have been observed at operation, but they are occasionally recognized by cholecystography. Vastine recorded 2 well illustrated examples which were detected by roentgenographic examination, the first of which was confirmed by operation. He pointed out that a calculus in such a diverticulum can be detected by its separation from, but its constant relation to, the gallbladder shadow. The gallbladder shadow also appears to be slightly indented at the base of such a diverticulum.

protrudes through on the upper convex surface of the liver. A bulge of the anterior portion of the right lobe has aroused suspicion of an intrahepatic gallbladder, and in some cases incision of this mass has penetrated into the gallbladder cavity. Less striking examples of buried vesicles are known to surgeons and pathologists who are familiar with partially and deeply embedded vesicles which are only partly exposed on their under-surface. The tip of the gallbladder is occasionally hidden in the substance of the liver, while the remainder of the organ is essentially free. In some instances the gallbladder is mostly exposed, but a bridge of hepatic tissue enfolds and completely encircles the body. The intrahepatic gallbladder is the extreme and more rare form of these

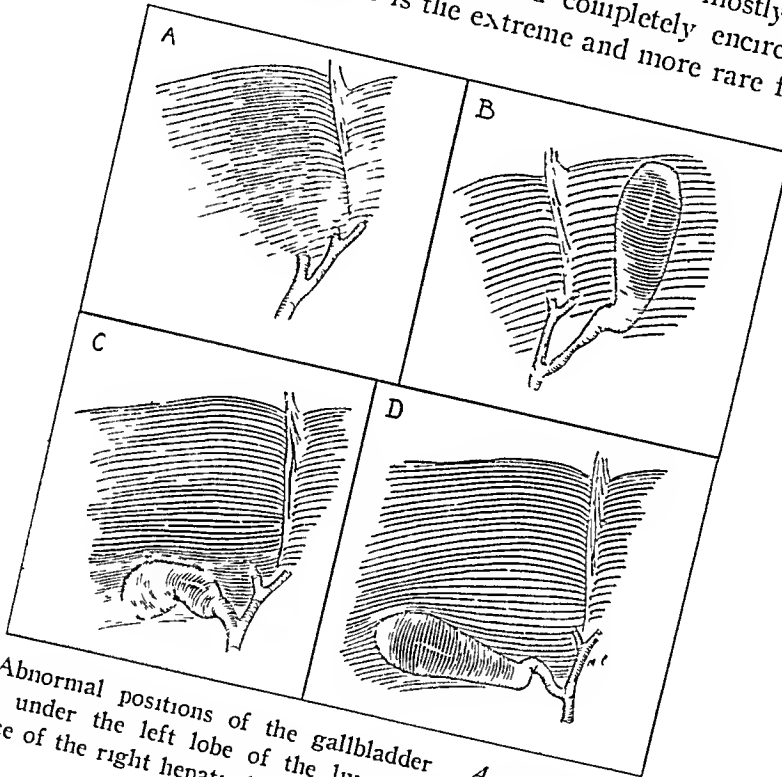


Fig 7—Abnormal positions of the gallbladder. *A*, within the substance of the liver, *B*, under the left lobe of the liver, *C*, on the posterior part of the inferior surface of the right hepatic lobe, and *D*, horizontally, within the transverse fissure.

variations. In the case of Walter and Neiman the distance between the surface of the liver and the buried gallbladder was from 3 to 4 cm, and no cystic duct was seen outside of the liver. The experience of Stetten demonstrated that an intrahepatic gallbladder containing stones is better treated by incision, removal of the stones and drainage than by removal of the gallbladder with its attending shock and hemorrhage.

*Gallbladder on the Left Side*—A gallbladder of this type has been described at least 7 times. In each instance the vesicle was situated

The origin of most diverticula of the gallbladder, particularly those occurring toward the neck, appears to be closely related to the development of the cysthepatic ducts. These small ducts, found in embryonic stages, pass from the gallbladder bud or from the upper portion of the cystic duct over to the substance of the liver. As the structures in the region assume their final size and relationships, these small cysthepatic ducts (when they persist) are found coursing between the neck of the bladder and the adjacent liver in the region of the fossa of the gallbladder. Such ducts are observed rarely in adult human beings, but Boyden has seen them in 25 calves and 2 pigs. An example in man is found in the case of Eisendrath (fig 6*B*), in which there was persistence of the

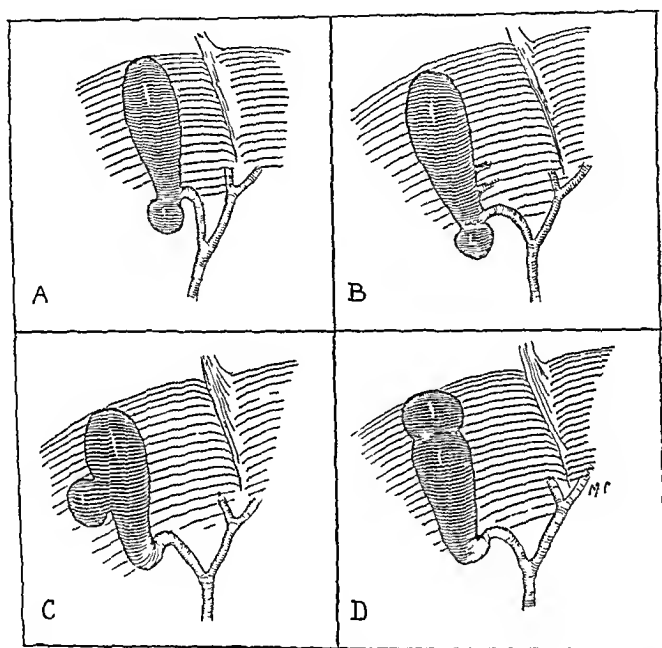


Fig 6—Forms of diverticula of the gallbladder. *A*, a diverticulum at the neck of the gallbladder, *B*, at the neck of the gallbladder, associated with persistent cysthepatic ducts which directly enter the gallbladder, *C*, of the body of the gallbladder, and *D*, at tip of the gallbladder.

cysthepatic ducts opening directly into the gallbladder. In this case a diverticulum was also present at the neck of the gallbladder. It is by persistence of these ducts, or from remnants thereof, that diverticula are believed to arise. While these ducts and early diverticula are thus present on that side of the gallbladder facing the liver, the normal rotation of the gallbladder may bring the diverticulum to lie on the exposed surface of the gallbladder (fig 6*A*).

To explain the origin of a diverticulum on the fundus of a gallbladder is difficult. Those fundic forms which are described as having a trans-

culties encountered in draining or removing stones from such an organ are obvious. Such a position of the gallbladder is probably attained by migration of the normally formed structure and an anchoring in this backward portion by the developing peritoneum.

*Transverse Position of the Gallbladder*—This condition has been described twice. In these 2 instances the gallbladder lay somewhat farther back than its normal position and was turned to assume a horizontal position within the transverse fissure (fig 7D). In Gay's case the gallbladder was barely one-third the normal size and lay in the extreme right of the transverse fissure, it was almost completely surrounded by the substance of the liver. Deaver and Ashhurst also described a gallbladder which was deeply placed and "horizontally transverse." Such a site for a gallbladder is again presumably dependent on an abnormal rotation or migration of the definitive organ.

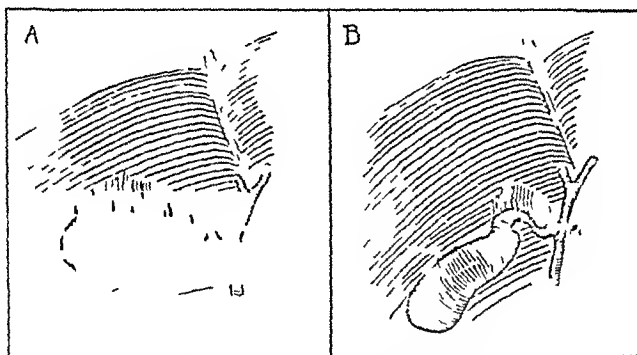


Fig 8—Floating gallbladders with a "mesentery." A, mesentery supporting the gallbladder and cystic duct, B, mesentery supporting only the cystic duct, allowing the gallbladder to hang free.

*Floating Gallbladder*—Torsion of the Gallbladder. As has been previously seen, the gallbladder may assume positions with varying degrees of partial or complete embedment within the liver. Of similar interest, but of greater importance from the standpoint of frequency of occurrence and liability to produce clinical symptoms, is the study of gallbladders which hang from the liver on a sort of "mesentery." The peritoneal coat surrounding such a gallbladder continues as two approximated leaves to form a fold or mesentery to support the gallbladder from the under-surface of the liver. This fold is of variable length and may allow the gallbladder to hang for as much as from 2 to 3 cm from the inferior hepatic surface. The fold may run the entire length of the gallbladder and cystic duct (fig 8A), or it may support only the cystic duct and allow the gallbladder to hang free and movable (fig 8B). Graded forms and combinations of this fold have been described, the

TABLE 4—Data in Cases of Absence of the Gallbladder

No of Case	Author	Year	Sex	Age, Yrs	Symptoms	Physical Findings	Pathologic Observations
1	Bubenhofer	1905	M	66	Died of cardiac failure		No gallbladder or cystic duct, no gallbladder fissure
2	Niemack	1908	F	60	Colicky pain in abdomen and right shoulder clay stools, fever	Jaundice fever	No gallbladder, stone in common duct
3	Stone	1908	F	54	Intermittent icterus and epigastric pain for 5 yrs	Poorly nourished, anemic	No gallbladder stones in hepatic and common ducts
4	Hinder	1909	M	60	Chronic discomfort after meals attacks of apparent cholecystitis		No gallbladder found, small dimple at edge of liver representing gallbladder fissure chronic pancreatitis and hepatitis
5	Eiben	1910	M	48	Nothing referable to biliary tract died of pneumonia		No gallbladder, no cystic duct, no gallbladder fissure
6	Eiben	1910	F	20	Died of phthisis		No gallbladder, cystic duct, gallbladder fossa or cystic artery common duct of normal caliber
7	Hoffman and Jackson	1910	F		Attacks simulating cholecystitis	Elderly patient	No gallbladder, common duct greatly dilated
8	Leopold	1911	F	45	Attacks of colicky epigastric pain with icterus for 17 yrs	Icterus stools pale	No gallbladder stones in hepatic and common ducts
9	Blakeway	1912	M		No symptoms from biliary tract, died of imperforate anus	Newly born infant	No cystic duct or gallbladder hepatic and common ducts not dilated no quadrate lobe of liver
10	Goebel	1913	F	60			No gallbladder stones in common duct
11	Ewers	1914	F	45			No gallbladder or cystic duct
12	Schulz	1914	F	60	Jaundice for 6 wks	Jaundice, enlarged liver	No remnant of gallbladder, large stone in common duct
13	Attridge	1918			Symptoms of obstruction of common duct		No gallbladder 2 stones in common duct
14	Muller	1920	F	28	Died of pneumonia		No gallbladder, cystic duct or gallbladder fossa, common duct of normal size
15	Naegeli	1921	F	34	Gallstone colic, vomiting, icterus and clay stools, in attacks for 5 yrs	Icterus, tenderness in right side of hypochondrium	No gallbladder no gallbladder fossa considerable dilatation of the common duct stone in right hepatic duct
16	Naegeli	1921	F	65	Gallstone colic radiating to shoulder vomiting and icterus for 30 yrs	Icterus, tenderness in right side of hypochondrium	No gallbladder stones in common and hepatic ducts
17	Knob	1922	F	1	No symptoms from biliary tract died of pneumonia and pleuritis		No gallbladder or gallbladder fissure, common and hepatic ducts normal in size
18	Fuld	1924	M	20	Died of pulmonary tuberculosis		No gallbladder or gallbladder fossa, no quadrate lobe
19	Giuliani	1924	F	35			No gallbladder, common duct contained stones and was dilated
20	Martin	1924	F	1	No symptoms from biliary tract died of bronchopneumonia		No gallbladder, slight groove present, marking right border of quadrate lobe
21	Jones	1926	F	3	Nothing referable to biliary tract died after rectal operation		No gallbladder



TABLE 5—Data in Cases of Abnormally Placed Gallbladders

No of Case	Author	Year	Sex	Age, yrs	Symptoms	Physical Signs	Pathologic Observations
Intrahepatic Gallbladders							
1	Déve	1903					Gallbladder within substance of right lobe of liver
2	Lemon	1905					Gallbladder entirely embedded within substance of right lobe of liver
3	Loughran	1905	M		No symptoms referable to biliary tract, killed in mine explosion		Normal sized gallbladder almost entirely embedded in hepatic substance, cystic duct partially embedded in hepatic tissue
4	Walter and Neilman	1931	F	27	Attacks of pain in right upper quadrant and nausea, occasional vomiting	Temp., 101.2 F	Liver incised and gallbladder found 2 stones removed, distance between surface of liver and gallbladder 3 to 4 cm, cystic duct in liver
5	Stetten	1933	M	45	Attacks of epigastric pain, fever and vomiting for 12 yrs, jaundice once	Tenderness in right subcostal area	Gallbladder entirely surrounded by hepatic substance, except for a small area on its superior aspect, stones in gallbladder
Left Sided Gallbladders							
1	Kehr	1902					Gallbladder under left hepatic lobe and situated to left of ligamentum teres, cystic duct entered left hepatic duct
2	Déve	1903					Gallbladder to left of ligamentum teres, opening of cystic duct not recorded
3	Walton	1902	F		Nothing referable to biliary tract died after prolonged labor	Newly born infant	Cystic duct started up toward right, then turned to left, to enter gallbladder which was to left of ligamentum falciforme
4	Kehr	1913	F	35	Colicky pain in right upper quadrant for 6 yrs radiating to back and loss of weight		Gallbladder under left lobe of liver and to left of ligamentum teres, stone in neck of gallbladder, opening of cystic duct (?)
5	Virenque	1923					Gallbladder under left hepatic lobe
6	Harris	1926	M	1 Mo	No symptoms referable to biliary tract, died of bronchopneumonia		Cystic duct started to right, then turned to left to join gallbladder bladder under falciform ligament with fundus to left of midline
7	Rolleston and McNece	1929					Gallbladder under left lobe of liver
Retrodplacement of Gallbladder							
1	Ferguson	1901	M	45	Gallstone colic, jaundice and fever for 4 yrs		Gallbladder not visible, stones palpable in gallbladder, gallbladder retroperitoneal, extending from vena cava upward, backward and outward
2	Ferguson	1901	M	75	Gallstone colic with colitis for 1 yr		Gallbladder not seen, felt on posterior edge of inferior surface of liver, behind peritoneum, stones
3	Mayo Robson						Gallbladder coursed downward and backward on posterior inferior surface of right hepatic lobe
4	Baldwin						Practically no left lobe to liver, gallbladder passed downward and backward lying just to right of vertebral column
5	Hofmann	1925	M	23	Colicky pain in region of gallbladder for 4 yrs		Gallbladder ran backward and downward toward kidney, lying in bed on undersurface of liver, cholecystitis and stones in gallbladder

no evidence of an inflammatory process in the gallbladder. One is especially convinced of the congenital origin of such a form when it occurs with associated atresia or malformation of the bile ducts. Many cases of hour-glass gallbladder in the adult have been described after cholecystographic examinations, but such examples should not be accepted unless confirmed by operation, because adhesions or extrinsic masses pressing on the gallbladder may produce the picture of this deformity in the roentgenogram. A phrygian cap gallbladder has been frequently described as a congenital malformation, and many examples are recorded in which this has been found by roentgenographic study. This puckering over of the tip of the gallbladder is usually, if not always, an acquired characteristic. A rudimentary gallbladder is occasionally described. When they occur in elderly subjects it is impossible to tell how much is attributable to scar formation. There are, however, small rudimentary gallbladders found in infants and in children which are little more than a nubbin and which undoubtedly represent a congenital hypoplasia.

Of interest to the surgeon, in spite of their apparent rarity, are those variations in the bile ducts in which accessory ducts enter the gallbladder directly from the liver via the bed of the gallbladder. Four examples of this may be cited. Kehr described 2 cases, in each of which two large ducts directly entered the gallbladder on that side which lay against the liver. Odermott described an additional case, in which a large accessory duct thus entered the gallbladder. The same condition is probably represented in the case of Desgouttes and Ricard, in which an accessory duct coursed from the liver directly over to the neck of the gallbladder. These accessory ducts are persistent cysthepatic ducts which communicate between the gallbladder and the liver proper in embryonic stages. It is not impossible that many of these ducts have been overlooked and have been cut across in the course of operations on the biliary tract, and the severance of such ducts might well explain some of the leakage of bile which is occasionally encountered from the bed of the gallbladder.

#### ANOMALOUS POSITIONS OF THE GALLBLADDER

Abnormal sites of the gallbladder are rare, but at least four such locations should be considered because of the interest they have had for surgeons and the technical difficulties they have sometimes presented at operation (fig 7).

*Intrahepatic Gallbladder*—A gallbladder of this type lies wholly within the substance of the right lobe of the liver and is surrounded by hepatic tissue, so that at first sight the vesicle may be thought to be absent (fig 7A). A small portion of the neck of the gallbladder may be visible, or a very small tip of the fundus may present as the gallbladder.

TABLE 6—Data in Cases of Bladder with Mesentery and Torsion of Bladder

No of Case	Author	Year	Sex Yrs	Age	Symptoms	Physical Findings	Pathologic Observation	Treatment and Result
1	Mayer	1908	F	51	Abdominal pain 2 days before hos- pitalization, no vomiting	Abdomen rigid lapse mass in right side of abdomen	Gallbladder infarcted twice on cystic duct, rotated gallbladder	Cholecystectomy, death
2	Mülhsem	1908	F	61	Pain in right side radiating to shoulder for 1 day	Abdomen spastic tender on right mass near umbilicus, white blood cells, 20,000	Gallbladder enlarged, red black and turned 360 degrees clockwise	Cholecystectomy, recovery
3	Nehrkorn	1909	F	71	Severe pain in right side and back for 8 days	Tender mass in area of gallblad- der larger than a fist	Gangrenous gallbladder hung free on pedicle, on which it was twisted	Cholecystectomy, recovery
4	I ett	1910	F	72	Sudden pain in right side of hypo- chondrium for 3 days, vomiting 4 or 5 times	Right side of hypochondrium very rigid and tender mass felt, temp, 101° F	Gallbladder black twisted twice mesenterly supported only cystic duct	Cholecystectomy
5	Flecher	1912	M	70	Repeated vomiting and pain in right side for 2 days, general ill health	Abdomen tense and spastic mass in right side of abdomen, looked very sick	Gallbladder black red and tense twisted 60 degrees in clockwise	Cholecystectomy death
6	Kubik	1913	M	73	Abdominal pain, nausea and vomit- ing	Rigidity in right upper quadrant epigastric mass, temp, 99° F	Gallbladder twisted 270 degrees, discolored, local peritonitis	Cholecystectomy
7	Cramp	1916	F	73	Digestive disturbances vague pain in upper part of abdomen vomiting for 3 days	Movable mass felt in right upper quadrant	Gallbladder twisted one and a half times counter-clockwise	No operation death
8	Schaeffer	1919	F	73	Epigastric pain, nausea and gas cons erections for 1 day	Right side of abdomen tender and resistant, pulse rate, 88	Gangrenous counter-clockwise well as cystic duct gallbladder as	Cholecystectomy
9	Reifel	1920	F	73	Severe abdominal pain and vomiting for 1 day, previous gallstone colic 4 days (occasional abdominal pain nausea and vomiting for 1 day)	Abdomen distended gallbladder enlarged, palpable and tender abdominal distention, tender, re- istance under liver	Fluid in abdomen, gallbladder as gangrenous, twisted 360 degrees discolored and gangrenous con- tained stones	Cholecystectomy recovery
10	Krabbel	1920	F	73	Acute onset of abdominal pain nausea and vomiting for 1 day	Mass tender mass in area of gall bladder	Gallbladder twisted 180 degrees and contained stones discolored	Cholecystectomy recovery
11	Hansen	1921	F	73	Abdominal pain and vomiting for 1 day, previous gallstone colic 4 days (occasional abdominal pain nausea and vomiting for 1 day)	Abdomen rigid, tenderness on right side of abdomen temp, 99° F	Fluid in abdomen gangrenous gallbladder twisted 360 degrees	Cholecystectomy recovery
12	Krabbel	1921	F	73	Severe epigastric pain and vomiting for 1 day	Mass felt in region of pylorus rigidity and tenderness especially in right upper quadrant, temp, 97.6° F	Gallbladder darkly colored, with loose adhesions turned 360 degrees on pedicle	Cholecystectomy recovery
13	Hansen	1921	F	73	Abdominal pain and vomiting for 1 day, previous gallstone colic 4 days (occasional abdominal pain nausea and vomiting for 1 day)	Mass felt in right upper quadrant, temp, 97.6° F	Gallbladder in cm long and 7 cm in diameter infarcted with several stones	Cholecystectomy recovery
14	Strauss	1921	F	73	Sudden severe abdominal pain and vomiting, ("stomach pain") for 1 day	Mass felt in right upper quadrant, temp, 97.6° F	Gallbladder black, edematous and distended, twisted 360 degrees	Cholecystectomy recovery
15	Frankau	1922	F	73	Colicky pain in upper part of ab- domen and incessant vomiting for 1 day	Mass felt in right upper quadrant, temp, 97.6° F	Gallbladder twisted 360 degrees discolored	Cholecystectomy recovery

on the under-surface of the left lobe of the liver (fig 7B) It was usually of essentially normal size, but in the first case of Kehr it was small The cystic duct of the gallbladder entered the left hepatic duct in 1 case, entered normally at the junction of the hepatic and the common ducts in 3 cases and had an unrecorded exit in the other 3 instances In all cases the gallbladder lay to the left of the round and falciform ligaments, and where the latter ligament was very broad the gallbladder was hidden from the operator's view through an ordinary incision in the right upper quadrant In none of the 7 cases was there any gallbladder in the fossa under the right hepatic lobe

A gallbladder can be developed to lie under the left lobe of the liver in one of two ways First, the ectopic gallbladder which had a normal exit for its cystic duct very likely arose as a normal embryologic bud from the hepatic diverticulum, but instead of assuming its normal position under the right lobe it migrated to a position under the left lobe It would therefore retain its normally implanted and attached cystic duct With the development of the peritoneum the gallbladder would be fixed in its position to the left of the falciform ligament Such an origin seems highly probable in cases such as those described by Walton and by Harris, in each of which the cystic duct arose from the junction of the hepatic and the common duct, was directed forward and to the right toward the normal fossa of the gallbladder and then took a sharp hairpin turn toward the left and passed behind the falciform ligament to communicate with the gallbladder on the left side A second way in which a gallbladder on the left side may be explained is as an independent development of a second gallbladder directly from the left hepatic duct, accompanied by a failure of development of the normal structure on the right side This appears to have been the process in the first example recorded by Kehr

*Retioidisplacement of the Gallbladder* —This abnormality is exemplified by 5 reports The gallbladder is not found in its normal position but has a cystic duct arising in the usual fashion from the extrahepatic system The gallbladder does not normally course forward and downward on the under-surface of the liver but instead leads upward and backward to gain the inferior and posterior portion of the liver (fig 7C) In Mayo Robson's case it was attached to the under-surface of the liver, but in Baldwin's case it passed downward and backward and lay just to the right of the vertebral column In Ferguson's first case the gallbladder was not visible, but it could be felt with a palpating hand as it lay retroperitoneally, extending along the vena cava in an upward, backward and outward direction In Ferguson's second case the gallbladder could not be seen, but it could be felt on the posterior edge of the under-surface of the liver and behind the peritoneum The diffi-

TABLE 6—Data in Cases of Bladder with Mesentery and Torsion of Bladder—Continued

No of Case	Author	Year	Sex	Age, Yrs	Symptoms	Physical Findings	Pathologic Observation	Treatment and Result
35	Marinacci	1926			Sudden onset of symptoms	Mass felt in region of gallbladder	Gallbladder distended, black, necrotic twisted on cystic duct	Cholecystectomy recovery
36	Busch	1927	F	75	Epigastric, intermittent pain for 3 days	Spasm and tenderness in upper part of abdomen, mass felt near umbilicus	Gallbladder enlarged, hemorrhagic and twisted	Cholecystectomy recovery
37	Carlsson and Wakeley	1927			Symptoms for 24 hrs		Gallbladder twisted on its hepatic attachment gangrenous	Cholecystectomy
38	Isau	1927	F	48	2 attacks of sudden illness, right epigastric pain, vomiting and collapse	Spasm and elongated mass in right lower quadrant	Fluid in abdomen gallbladder edematous and thickened, twisted 90 degrees	Cholecystectomy, recovery
39	Isau	1927	F		Severe, 24 hr attack of pain and vomiting		Gallbladder hung free from surface of liver mucosa necrotic	Cholecystectomy
40	Holden	1927	M	49	Abdominal distention, nausea and subsequent epigastric pain for 1 day	Right subcostal rigidity and tenderness, white cell count, 11,400	Gallbladder black and gangrenous, twisted on its cystic duct 1½ times	Cholecystectomy, recovery
41	Shipley	1927	F	65	Sudden onset of continued epigastric pain, radiating to back for 2 days	Looked ill entire abdomen rigid, temp, 100 F, pulse rate, 100	Seroanginous abdominal fluid gallbladder smooth and black, torsion 360 degrees	Cholecystectomy recovery
42	Therstappen	1928	F	80	Abdominal pain, especially on right side, for 2 days	Emaciated, tender mass under right subcostal margin	Gallbladder turned three complete revolutions solitary stone in gallbladder	Cholecystectomy, recovery
43	Mcade	1929	F	36	Recurring pain on right side of abdomen for 1 day	Rigidity and tenderness of abdomen, especially over appendix	Fluid in abdomen gallbladder distended and gangrenous, rotated three times	Cholecystectomy recovery
44	Costantini	1930		42	Diffuse abdominal pain, especially in area of gallbladder, with vomiting	Spasm and pear-shaped mass, in right side of hypochondrium, pulse rate, 120	Green black, edematous gallbladder, twisted on pedicle	Cholecystectomy
45	Gwynne	1930	F	77	Sudden severe pain in right subcostal area, with nausea and vomiting	Tender, pyriform mass in right side of hypochondrium moved with respirations	Gallbladder reddish purple twisted clockwise 180 degrees	Cholecystectomy recovery
46	Kettner	1930	F	53	Sharp sudden pain in right side of epigastrium associated with vomiting	Mass in right upper quadrant pulse rate, 100	Gallbladder hemorrhagic gall bladder contained stones twisted 180 degrees	Cholecystectomy
47	Wakeley and Hunter	1930			Severe colic		No infarction colic relieved by removal of bladder with mesentery	Cholecystectomy, recovery
48	Wakeley and Hunter	1930			Severe colic		No gangrene of gallbladder symptoms relieved by removal of gallbladder	Cholecystectomy, recovery
49	Wakeley and Hunter	1930			Symptoms for 24 hrs		Gallbladder twisted on attachment and gangrenous	Cholecystectomy
50	Murray	1933	M	83	Unabating pain in right upper quadrant, with frequent vomiting, for 2 days	Tenderness and rigidity in right side of hypochondrium white cell count, 22,000	Bloody fluid in abdomen gangrenous gallbladder twisted 540 degrees	Cholecystectomy death

classification being based on the length of the fold and the amount of the gallbladder which is supported thereby. In different series of investigations the number of gallbladders possessing this supporting membrane has been listed as high as 4 to 5 per cent of dissecting room specimens.

It is not difficult to foresee the clinical significance of this anomaly for an organ which is so freely movable is apt to become twisted, and infarction will supervene from impairment of the blood supply in the small pedicle. Cases of this sort have been frequently listed in the literature, and 50 examples are listed in table 5 for summary and study. All cases with a gallbladder "mesentery" are too numerous for listing, hence only those have been included in which there was torsion of the gallbladder and operation or autopsy has been performed because of this condition.

The clinical symptoms of torsion of the gallbladder are strikingly similar from case to case and strongly suggest the proper diagnosis. This torsion is most frequently seen in women in the upper age groups. Of these 50 cases, 84 per cent were in women and 16 per cent were in men. The average age of the patients was 59 years. Of the 50 patients, 8 per cent were in the age group between 50 and 60 years, 16 per cent in the age group between 60 and 70, and 34 per cent in the age group between 70 and 80, 2 patients were over 80.

The patients are almost always thin, ptotic persons. The symptoms related to torsion of the gallbladder have an abrupt, rapid onset and continue with extreme severity. Intense and constant pain in the right upper quadrant ushers in the attack and is present during the entire length of the illness. Pain is rarely described as being transmitted to the back or to the right shoulder. Nausea and vomiting are always marked. Collapse is frequently encountered. The temperature, if at all elevated, is rarely over 100 F, but commonly the pulse rate is rapid and ranges between 100 and 120 or even as high as 150. The severity of the symptoms naturally predicates symptoms of short duration, and the history is rarely of more than from twenty-four to forty-eight hours' standing. Oddly enough, there is usually only one attack from this condition. One would expect, with a freely movable organ, that there might be minor episodes of abdominal pain, vomiting, etc., from temporary twists of the vesicle, but such does not seem to be the case. In only 5 cases was there any previous complaint which might have been attributable to torsion of the gallbladder and spontaneous relief. In the majority of instances, then, the patient has only one attack of torsion of the organ.

Physical examination shows an elderly, thin patient, usually a woman. Exhaustion is common. Tenderness in the right upper quadrant and spasm are the rule. The gallbladder is often palpable (54 per cent of

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TABLE 5—Data in Cases of Abnormally Placed Gallbladders—Continued

No of Case	Author	Year	Sex	Age, yrs	Symptoms	Physical Signs	Pathologic Observations
Transversely Placed Gallbladders							
1	Gay	1902	M	27	No symptoms referable to biliary tract died of nephritis and endocarditis		Gallbladder ( $\frac{1}{4}$ normal size) in extreme right of transverse fissure of liver and almost surrounded by hepatic tissue
2	Deaver and Ashhurst	1914	M	38	Pain in area of gallbladder with jaundice for 4 yrs		Gallbladder deeply placed in horizontally transverse position calculi in gallbladder, cystic duct and in common duct

the cases) The twisted gallbladder is usually felt just below the edge of the liver, but because of its mobility it is sometimes felt in other parts of the abdomen, as in the right lower quadrant or in the umbilical region. A temperature of over 100 F is rare, unless the gallbladder has ruptured and peritonitis has set in. When the white blood cell count has been listed, it has ranged up to 18,000 and 20,000. In cases uncomplicated by peritonitis, the white blood cell count and the pulse rate are much higher than might be expected with the associated temperature.

At operation the gallbladder is found to be twisted on its pedicle in an arc varying from 90 to 1,080 degrees. Torsion of from 180 to 360 degrees is most often described. With the twisting of the pedicle the cystic artery and vein are occluded or compressed, and infarction of the gallbladder results. The wall of the gallbladder is therefore swollen, edematous, hemorrhagic and necrotic. Hemorrhagic fluid is occasionally found within the peritoneal cavity, and fibrinous exudate is usually deposited on the surrounding structures. The nature of the congenital anomaly makes surgical relief easily and quickly possible, for no dissection of the bed of the gallbladder is necessary. Rapid placement of clamps and ligatures on the vesicle stump and vessels is all that is required before the gallbladder can be cut from its pedicle.

The operative results in this condition have been very promising. Of the 47 patients operated on, 70 per cent recovered and 15 per cent died; the outcome in the remaining cases is not stated. These results are especially noteworthy in view of the age of these persons.

The occurrence of torsion of the gallbladder in elderly persons is peculiar in view of the fact that the gallbladder has been freely movable during the entire life of these patients. The onset of torsion is probably delayed until later decades, when supporting fat has largely disappeared from the surrounding structures and when atrophy of the tissues allows for greater ptosis of the viscera, including the floating gallbladder. These two factors tend to increase the mobility of such a gallbladder and enhance the possibility of torsion.



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17	Ormos	1922	F	71	'Died with symptoms of hemorrhagic colitis		Greatly enlarged, necrotic gall bladder turned 450 degrees, peritonitis	No operation, death
18	Ionnas	1923	F	67	Sudden onset of generalized abdominal pain, vomiting and collapse	Sausage shaped mass felt below liver	Gallbladder enlarged and black twisted 2½ turns, stones in gallbladder	Cholecystectomy, recovery
19	Dubs	1924	F		Sudden onset of abdominal pain	Elderly patient pear shaped mass in area of gallbladder	Enormous, movable gallbladder, with narrow mesentery twisted on duct	Cholecystectomy, recovery
20	Dauv	1925	F	11	Sudden onset of generalized abdominal pain and frequent vomiting	Abdominal spasm, temp, 99 F, pulse rate, 112	Gallbladder distended and black, peritonitis, twisted 180 degrees clockwise	Exploration only, death
21	Jiffeld	1925	F	34	Sudden onset of severe pain right upper quadrant and vomiting for 2 days	Tenderness rigidity and mass in right upper quadrant	Gallbladder black, distended and very mobile, rotated once	Cholecystectomy recovery
22	Fischer	1925	F	44	Attacks of pain in back and right shoulder with vomiting for 3 yrs	Tenderness over area of gall bladder	"Mesentery" 45 cm long and 2 cm high, gallbladder twisted 90 degrees	Cholecystectomy recovery
23	Fischer	1925	F	29	Attacks of pain in epigastrium, back and right shoulder	Marked tenderness in right side of epigastrium	Gallbladder hung 3 cm below liver, twisted 90 degrees	Cholecystectomy recovery
24	Juttaud	1925	F	56	Sudden pain in right side of hypochondrium	Tender, tense, mass felt on right side of abdomen	Gallbladder had double twist	Cholecystectomy, recovery
25	Sutter	1925	F	62	Symptoms of incarcerated umbilical hernia for 1 day	Tense mass in umbilical hernia	Gallbladder on mesentery, twisted 180 degrees	Cholecystectomy, recovery
26	Sutter	1925	F	72	Recurring abdominal pain and vomiting for 6 days	Movable fist sized tumor on right side of abdomen	Tensely filled, pedunculated gall bladder, twisted 360 degrees	Cholecystectomy, recovery
27	Sutter	1925	M	71	Pain in right upper quadrant for years, especially when lying on left side	Slight tenderness over area of gallbladder	Gallbladder filled with stones freely movable, twisted 90 degrees	Cholecystectomy recovery
28	Feldmann	1926	F	46	Sudden epigastric pain and vomiting	Marked spasm and tenderness in right abdomen temp, 99 F, white blood cells, 18,000	Gallbladder size of "infant's head," and infarcted twisted 180 degrees	Cholecystectomy, recovery
29	Feldmann	1926	F	74	Acute onset of epigastric pain and vomiting	Spasm and tenderness in right epigastrium, obese temp, 99.5 F	Gallbladder dark red, infarcted, twisted 180 degrees	Cholecystectomy, recovery
30	Grunert	1926	F	66	Attack of abdominal pain 3 days previously (gallstone colic for 15 yrs)	Fist sized tender mass in right upper quadrant leterus	Gallbladder hemorrhagic, twisted 180 degrees, stones in gallbladder and common duct	Cholecystectomy recovery
31	Grunert	1926	F	67	Illness with severe uneasing pain in right epigastrium and vomiting for 2 days	Fist sized, tender mass in right side of abdomen, temp, 99.8 F pulse rate, 110	Fluid in abdomen bladder gangrenous, twisted 360 degrees, stones	Cholecystectomy death
32	Huddy	1926	F	71	Sudden onset, right sided pain for 2 days (bilious attacks for 17 yrs)	Tenderness, rigidity and mass about umbilicus temp, normal	Gallbladder twisted once, ant clockwise	Cholecystectomy
33	Lenckel	1926	M		Pain in right side of hypochondrium for 4 days, relief if patient remained quiet	Elderly patient tenderness in right upper quadrant	Gallbladder infarcted and gangrenous	Cholecystectomy, death
34	Lenckel	1926	M	76	Sudden pain in right upper quadrant and collapse less when patient quiet	Tenderness in region of gallbladder	Gallbladder gangrenous	Cholecystectomy, death

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## SUMMARY

One hundred forty-seven cases of congenital anomalies of the gallbladder are selected from the literature for review. A case of double gallbladder is reported.

The presence of a double gallbladder has been recorded 28 times in man. The accessory bladder may be contiguous to the normal organ, under the left lobe of the liver, partially within the substance of the liver or rarely along the gastrohepatic ligament.

A bilobed gallbladder has been occasionally described in man. This may have the form of a single organ, divided by an internal central septum, or more often has a V shape (with the two cavities joined only at their junction with the cystic duct).

A diverticulum of the gallbladder may occur along the free surface of the organ from the neck to the fundus, and in 1 instance a diverticulum was described on the hepatic side of the gallbladder.

Thirty-eight cases of absence of the gallbladder are listed in which there was no other anomaly of the liver or biliary system. (Approximately 35 other cases of absence of the gallbladder have been recorded in which there was associated congenital atresia of the extrahepatic ducts.)

A normally formed gallbladder has been found in the following anomalous positions: within the substance of the liver, under the left lobe of the liver, posteriorly under the inferior aspect of the right hepatic lobe and horizontally in the transverse fissure of the liver.

A "floating gallbladder," because of its suspension by a "mesentery," is likely to become twisted and infarcted. The resultant gangrene of the gallbladder is productive of severe clinical symptoms and necessitates immediate operation. Surgical removal of the organ leads to recovery in most instances if operation is performed before peritonitis supervenes.

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rately in the first case. The kidney was enlarged, soft and definitely hydronephrotic, and the pelvis was dilated. The ureter was dilated throughout. Within  $1\frac{1}{2}$  inch (3.5 cm) of the lower end of the ureter there was a sausage-shaped swelling which measured approximately 2 inches (5 cm) in length, and  $\frac{3}{4}$  inch (2 cm) in diameter, it was moderately firm, and the bulk of this mass could be moved inside the ureter. The ureter was opened from end to end and revealed a villous tumor practically occluding the lumen. In the second case nephro-ureterectomy was performed also. The distal 5 cm of ureter was dilated to 1.5 cm in diameter. This portion was firm, and there was apparently a tumor either within the lumen or within the walls of the ureter. The upper extremity of this dilated portion was 8 cm from the kidney, a grayish-red, papillomatous-appearing growth 3 cm long and 1 cm in diameter, of the shape of a date stone, was found, it was growing from a narrow pedicle attached to the wall of the ureter at the upper extremity of the growth, hanging downward in the lumen of the ureter. In the third case, a fusiform enlargement was found in the lower portion of the ureter, extending down to the junction of the ureter and the vas deferens. Beyond this point the ureter lessened in size until it became of normal caliber. The lower end was ligated and severed at its entrance to the bladder. The upper end was ligated at the highest point possible and cut across. The intervening portion of ureter was removed. This tumor was shown by microscopic section to be a primary papillary carcinoma of the ureter.

Primary tumors of the ureter are rare. Although secondary extensions from papillary carcinomas of the renal pelvis are common, only 61 cases of primary carcinoma have been reported.

Ravich<sup>37</sup> described a case of neurofibroma of the left ureter in a man aged 50, whose chief complaint was pain in the left lumbar region, with extension to the genital region. Examination gave evidence of obstruction of the left ureter in its upper third, with advanced hydronephrosis and a periureteral mass demonstrable by roentgenograms. A diagnosis was made of ureteral tumor, and at operation a mass was found surrounding and obstructing the ureter in its upper third. Section proved it to be a neurofibroma. Nephro-ureterectomy resulted in cure, for the patient was living and well at the time of the report, four years after operation.

Although neurofibromas have been reported as occurring in almost every other organ of the body, the aforementioned report is the first one of neurofibroma involving the ureter.

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tomy The chief complication is sloughing of the ureter The mortality is less than with uretero-enterostomy Uretero-enterostomy is especially suitable in case of exstrophy and vesicovaginal fistula It is less suitable in cases of cancer of the bladder, largely because of the lowered resistance of the patient and the likelihood of dilatation of the ureter and pre-existing urinary infection The late results of uretero-enterostomy are still sub judice This phase of the subject has not been thoroughly studied, but a number of cases have been reported in which renal calculi and pyelonephritis have developed

*Injuries*—In the treatment of operative injuries of the ureter the problem varies with the time since the injury, the distance of the injured portion from the bladder, the involvement—whether of one or both ureters, and the type of injury, that is, whether the ureter is completely severed, completely severed with removal of a segment, partially severed, ligated or whether it has been clamped

When confronted by this accident many surgeons ligate the proximal end of the severed ureter This practice is to be severely condemned when circumstances are favorable for repair Its late results are a functionless kidney or hydronephrosis, its immediate complications may be urinary leakage and extravasation, peritonitis, urinary fistula or renal infection necessitating further surgical intervention

Sisk<sup>41</sup> has used a simple method of immediate repair which was independently described by Young A ureteral catheter as large as will freely move through the ureter without interfering with the circulation is introduced into the ureter and passed into the renal pelvis Introduction may be made through a cystoscope, or the catheter may be passed each way from the point of injury, the lower end being brought out through the urethra later on Over this catheter, end-to-end anastomosis is made with fine catgut, the sutures being passed through the serous and muscular layers With satisfactory drainage the catheter may be left in place for many days to prevent contraction of the lumen during healing

Exceptions are to be made (1) when the injury is sufficiently low to permit reimplantation into the bladder, which is preferable, or (2) when a segment of sufficient length to cause tension has been removed If there is tension satisfactory healing will not occur, and implantation into the bowel is the operation of choice

In cases of old injuries complete studies are necessary to determine the advisability of plastic repair, of implantation into the bladder or bowel, of nephrostomy or of nephrectomy

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- Toida, R Ueber einem Fall von grosser congenitaler sanduhrformiger Gallenblase, *Arch f klin Chir* **100** 1188, 1913



Chemicals producing tumor are encountered in the intermediate stage of manufacture. Careful analysis indicated that beta naphthylamine, benzidine and alpha naphthylamine are the causative materials. In repeated examinations of a group of patients exposed to aniline only over a period of eighteen years there was no incidence of tumor, this makes it seem possible that aniline is at least a questionable factor. The period of exposure varied from five to twenty-three years, the average being eleven years. German observers have reported 1 case in which the tumor appeared after as short a period of exposure as two years, there was no evidence in this instance, however, to indicate that the patient had a normal bladder when he began to work with the chemicals. Age does not seem to bear any direct relationship to incidence. In this group 1 patient was 24 years of age, 9 were from 30 to 40, 13 were from 40 to 50, and 12 were from 50 to 60 years old.

Absorption takes place by the respiratory, gastro-intestinal and cutaneous routes. The most important route is the respiratory one, but it should be borne in mind that cutaneous absorption of intermediates can, under conditions of careless handling, become the most significant portal of entry.

Gehrmann stated that to prevent the disease the manufacture of dye intermediates must be conducted in such a manner as absolutely to exclude dust, fumes and contact of offending substances with the skin. This means that there must be an entirely closed process for the manufacture of alpha and beta naphthylamine, benzidine and aniline. Tumors classified as of grade 1 malignancy, which are small and easily accessible, are treated by bipolar fulguration through the cystoscope. Large tumors of grade 1 are treated by open operation. Tumors of grade 2 malignancy, which are reasonably small and easily accessible, are treated through the cystoscope by fulguration. Open operation should be performed in cases of large and inaccessible tumor. Open operation and implantation of radon seeds is the method to be used in treatment of all tumors of grade 3 or 4 malignancy.

Pfahler and Vastine<sup>45</sup> stated that tumors of the bladder varying from 1 cm in diameter to a large size can be demonstrated clearly by means of pneumocystograms. Progressive enlargement or progressive reduction in size of this lesion can be shown and recorded photographically. The method of examination is comparatively painless and harmless. During treatment by high voltage roentgen therapy the progressive disappearance of the tumor may be recorded serially from time to time.

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<sup>45</sup> Pfahler, G. E., and Vastine, J. H. The Roentgen Diagnosis and Treatment of Tumors of the Bladder. Their Serial Study with Pneumocystograms, Showing Results of Treatment by Irradiation, *J. A. M. A.* **104** 609 (Feb. 23) 1935.

## A REVIEW OF UROLOGIC SURGERY

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*(Continued from p 1042)*

### URETER

*Tumor* —Mathe and De La Peña<sup>35</sup> stated that early diagnosis of primary carcinoma of the ureter affords the only opportunity of cure by early surgical removal. The possibility of this lesion should be considered in patients who have the general symptoms of cancer, who present the triad of hematuria, lumbar pain and tumefaction of the kidney, in whom obstruction of the ureter is encountered and in whom the possibility of the presence of stone, stricture of the ureter and tumor of the kidney can be definitely eliminated. Salient points in establishing a positive diagnosis are the presence of a tumor projecting from the orifice of the ureter or in the adjacent mucosa, an impassible obstruction in the ureter, modification of the ureteral spurt, nonperistaltic hematuria resulting from attempts to pass with a catheter, and a filling defect of the ureter, as revealed by urogram, with hydro-ureter and hydronephrosis above the point of pressure. The treatment of choice is complete nephro-ureterectomy, when feasible, including removal of the intramural portion of the ureter in one operation.

Hunter<sup>36</sup> reported 2 cases of primary carcinoma and 1 of benign papilloma of the ureter. The kidney and ureter were removed sepa-

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35 Mathe, C P, and De La Peña, Emilio. Primary Carcinoma of the Ureter, California & West Med **42** 357 (May) 1935

36 Hunter, A W. Primary Tumor of the Ureter. End Results in Three Cases, J Urol **33** 443 (May) 1935

ation on the prostate gland. It occurs more frequently after perineal than after suprapubic prostatectomy, or resection of the prostate gland. Development of this condition following prostatectomy is attributable to total destruction or derangement of both the internal and the external sphincter of the bladder. In cases of complete or partial incontinence following this operation, various anatomic defects or pathologic lesions about the posterior urethra and neck of the bladder may be associated with loss of function of both sphincters.

Satisfactory results have been obtained in treatment of this condition, in female and in male patients, by transplantation of the gracilis muscle. In the 2 cases of complete incontinence of urine following perineal prostatectomy reported by Abeshouse, the operative technic employed was originally described by Player and Callander. In one instance complete control of urine during the day and the night was restored. In the other case complete control of urine was restored during the night and in the reclining posture, but there was partial diurnal incontinence when the patient assumed the upright position and after excessive muscular effort. It is important and necessary that the urine be diverted from the field of operation. Drainage of urine through an indwelling urethral catheter may suffice in certain types of incontinence of female patients, who are treated by extravesical plastic operations on the sphincters of the bladder and urethra or by transplantation of a voluntary muscle or fascia. However, this type of drainage is usually inadequate and inefficient in similar cases of incontinence of male patients. Drainage of urine by means of suprapubic cystotomy, performed preferably several days previous to transplantation of the muscle, has the advantages of permitting excoriation of the skin about the external genitalia to clear up, minimizing the subsequent influence of such cutaneous lesions on development of an infection in the region of the operation, keeping the operative field dry during and after transplantation of the muscle and facilitating primary healing by eliminating the irritative and infectious tendency of an indwelling urethral catheter.

Deming<sup>49</sup> stated that the fact that 9 cases of simple transplantation of the gracilis muscle have been reported by six different surgeons, with good results in 8 and no deaths, indicates that this plastic procedure has definite merit. The 1 failure was attributable to incorrect application of the procedure and not to the operation itself. The indications for use of the method may be considered to be present when the sphincters of the bladder are absent or vary from normal and there is a good detrusor urinae muscle of the bladder. It should not be used when the detrusor

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<sup>49</sup> Deming, C. L., in discussion on Watson, E. M. Complete Rupture of the Urethra, *J. Urol.* **33**: 73 (Jan.) 1935.

*Stone*—Foley<sup>38</sup> stated that the management of stone of the ureter by expectancy and manipulation has been employed too extensively. The morbidity, mortality and hardships are underestimated, and the just purpose of such methods is often subordinated to zeal for their use. They are conservative only when they serve the patient's welfare.

Lumbar ureterotomy should always be of more minor character than pelvic ureterotomy. This fact is not properly recognized. It should always be taken into account in determining between expectancy and manipulation on the one hand and open operation on the other. Lumbar ureterotomy as usually described and observed, is a major operation and does not properly take advantage of anatomy, toward the ends of simplicity, accuracy and minimal trauma. The improved methods for this procedure, however, take advantage of anatomy toward these ends, and this greatly minimizes the operation. A lumbar stone of the ureter, 5 mm or more in diameter, should be removed immediately by lumbar ureterotomy. Only minute stones should be allowed to pass into the pelvic ureter for spontaneous passage or manipulative removal.

Engel<sup>39</sup> stated that the multiplicity of methods advocated for manipulative removal of stones of the ureter is proof of the inadequacy of any one procedure. He has employed multiple catheters, the spiral stone extractor and dilation of the ureter below the stone with bougies and has been impressed with the infrequency with which the stones have been satisfactorily removed by these means. In his experience manipulative procedures often cause sharp reactions associated with chills, fever and rather marked prostration. Manipulation may traumatize the ureter and mucosa of the ureter sufficiently to produce stricture. Additional disadvantages are the prolonged period that is usually necessary to secure passage of the stone, during which time the patient is in fear of recurrent colic, and the period of morbidity is increased by the manipulative procedures. Open operation is often necessary after the patient has been exhausted by the preliminary procedures. Open operation for removal of stones in the ureter has been favored by Engel in the majority of instances. The situation of the calculus is important and should be considered when the decision as to treatment is made.

*Transplantation*—Smith<sup>40</sup> stated that diversion of the urinary stream is indicated in exstrophy of the bladder, in cases of intractable submucous cystitis, in certain cases of vesicovaginal fistula, in a few cases of tuberculosis of the bladder, and in selected cases of carcinoma of the bladder. Ureterostomy is particularly suitable in conjunction with total cystec-

38 Foley, F. E. B. Management of Ureteral Stone. Operation Versus Expectancy and Manipulation, *J. A. M. A.* **104** 1314 (April 13) 1935.

39 Engel, W. J., in discussion on Foley<sup>38</sup>.

40 Smith, G. G. Diversion of the Urinary Stream, *J. Urol.* **33** 179 (Feb) 1935.

part could be injured only in the event of forcing the outer end of the instrument up toward it, which is well-nigh impossible because the surgeon could not depress the hand holding the instrument far enough toward the abdominal cavity

This method of drainage has been of great help in numerous cases, and if there is no longer need for draining, the tube can be taken out. The channel of from 3 to 4 mm diameter left by it contracts entirely within a few days and closes without leaving the slightest tract.

*Use of Catheter*—Wesson<sup>51</sup> stated that an overdistended bladder, in which there is no obstruction, will never tear without external violence, hence, there is no danger of a cord bladder rupturing spontaneously. With a small quantity of morphine, and patience, the bladder will overflow and become automatic within ninety-six hours. Wesson cited 22 cases which illustrate the increased morbidity and financial cost resulting when the problem is complicated by infection from the use of a catheter. He does not consider it advisable to convert a typical neurosurgical case into a urologic one by the routine use of a catheter.

#### VESICOVAGINAL FISTULA

Kirwin and Lowsley<sup>52</sup> reported a study of treatment in 60 cases of vesicovaginal fistula as seen at the New York Hospital between 1844 and 1933 and concluded that this lesion is one of the most difficult to cure known to surgery. The first satisfactory technic was devised by Marion Sims in 1852, and that procedure, with slight modification to take advantage of certain new methods, is applicable at present.

Kirwin and Lowsley reported the case of a patient treated at the Brady Foundation for Urology of the New York Hospital, the sixty-first in a series from that hospital. The fistula was complicated by complete eversion of the bladder into the vagina, so that the everted bladder protruded at the vulva. The condition was treated in two stages. The features of the technic to be emphasized are the excision of all devitalized tissue, the bladder being incised almost to the edge of the fistula, the silver wire sutures used were similar to those used by Sims eighty years ago, and the suprapubic counterdrainage, with suction, permitted healing of the freshened edges of the fistula, which were uncontaminated by contact with urine.

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51 Wesson, M. B. Is the Use of a Catheter Ever Justified in Fractures of the Spine? *Urol & Cutan Rev* 38 572 (Aug) 1934.

52 Kirwin, T. J., and Lowsley, O. S. Radical Relief of Vesico-Vaginal Fistula. Report of an Unusual Case of Eversion of the Bladder Through the Fistulous Opening, and a Review of Sixty Cases Seen at New York Hospital During the Past Ninety Years, *J Urol* 33 51 (Jan) 1935.

Sisk reported 5 cases of operative injury of the ureter, in the first of these the operative repair described was successful, as was proved by re-examination five years after the injury

Follow-up studies are necessary, for absence of symptoms is no criterion of a satisfactory result

*Physiology*—Ockerblad, Carlson and Simon<sup>42</sup> studied the effect of morphine on the intact ureters of 24 patients. They made hydriophographic tracings by Trattner's method, and some of the patients were subjected to roentgen examination. Morphine given subcutaneously in the usual clinical doses was found to increase markedly ureteral tone and the amplitude of the contractions, the larger the dose, the greater the effect. The effect is produced by morphine in from two to five minutes and persists for at least three hours and probably longer. Atropine in doses of  $\frac{1}{100}$  grain (0.0006 Gm.) invariably eliminates the contractions of the ureter that is stimulated by morphine with a consequent loss of tone but does not act strikingly or constantly when given alone. The belief that morphine quiets the ureter is incorrect, instead it acts as a stimulant.

*Compression*—Baker and Lewis<sup>43</sup> compared the urographic outlines as obtained for pregnant women and for patients with tumor of the pelvis. They found a high degree of dilatation of the upper part of the urinary tract in pregnant women, in patients with large ovarian cysts and in patients with fibromas of the uterus. Dilatation of the right ureter and pelvis was much greater and more common than dilatation on the left side. The investigators are of the belief that the cause of dilatation is mechanical pressure and that the reason dilatation in the left tract is not as great as in the right is that the sigmoid acts as a cushion to protect the left ureter from direct pressure. The sigmoid causes torsion of the uterus with resultant increased pressure on the right ureter.

#### BLADDER

*Carcinoma*—Gehrmann<sup>44</sup> stated that the tumor of the bladder resulting from the handling of aniline is an entirely new occupational disease in this country, the first cases appeared in 1931. The patients who were examined had been engaged in the manufacture of dye intermediates. There was a total of 49 tumors—35 papillomas and 14 carcinomas. The incidence of tumor of the bladder was 4.1 per cent in the group of patients examined.

42 Ockerblad, N. F., Carlson, H. E., and Simon, J. F. The Effect of Morphine upon the Human Ureter, *J. Urol.* **33** 356 (April) 1935.

43 Baker, E. C., and Lewis, J. S., Jr. Comparison of the Urinary Tract in Pregnancy and Pelvic Tumors, *J. A. M. A.* **104** 812 (March 9) 1935.

44 Gehrmann, G. H. Papilloma and Carcinoma of the Bladder Among Dye Workers, *Surg., Gynec. & Obst.* **60a** 555 (Feb.) 1935.

*Carcinoma*—Barringer<sup>51</sup> stated that a comprehensive review of carcinoma of the prostate gland is most confusing and that it is practically a fatal disease. In 351 consecutive cases there were but 16 (4.5 per cent) carcinomas which might be called reasonably small that were confined to the region of the prostate gland and to the periprostatic region. Twenty-six (7.4 per cent) of the carcinomas were classified as of medium size, that is, reaching well beyond the prostate gland proper, but not too large and entirely within reach of the examining finger. In the remaining 309 cases (88 per cent) the carcinomas were extensive, that is, the tumor itself was large or, if the tumor was not large, the extensions around the seminal vesicles or to the lateral pelvic walls were definite, the bladder was secondarily involved, the tumor arose postoperatively or metastasis to bone or other structures was present. However, according to Barringer, there are some rays of hope, 29 (little more than 8 per cent) of his patients were well for periods varying between three years and seventeen years and ten months. The prostatic condition was such as to make one believe that the carcinoma was controlled. Nine patients went from three to five years without recurrence, 16 had no recurrence in from five to ten years, and 4 were well for more than ten years. Time alone will prove whether all these patients are cured. Transurethral resection of the prostate gland has made a great advance in coping with urinary retention, while irradiation, by radium, of the prostate gland has developed and become sufficiently accurate to enable one to irradiate a prostate gland without severe pain to the patient. External irradiation in sufficient quantity to be of any use has been employed only in the last few years. Cases of prostatic carcinoma are divided, for purposes of treatment, into classes. In the first class are those in which there is a reasonably small carcinoma of the posterior lobe with, as far as can be determined, no involvement of the other lobes and no urinary retention. The patients should receive irradiation by gold-screened needles inserted through the perineum into the prostate gland. They should, in addition, receive external irradiation. The two courses of irradiation are given as nearly simultaneously as possible. In the second class are cases in which urinary retention is the dominant symptom and in which there is involvement of the so-called median or of the lateral lobes. In these cases a suprapubic opening should be made, all obstructing portions of the prostate gland being cut out with electric cautery and gold seeds being implanted into the entire cancerous region, in exactly the same manner as gold seeds are implanted in vesical carcinomas. When the suprapubic wound heals the posterior lobe has to be carefully watched by means of palpation and possibly biopsy of aspirated material. If any

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54 Barringer, B. S. Prostatic Carcinoma, *J. Urol.* **33** 616 (June) 1935

Barringer<sup>46</sup> stated that up to a year ago there were two methods of treatment of cancer of the bladder. One was removal by operation, the other was application of radium suprapubically or through the cystoscope. Barringer favors treatment with radium. It can be used in cases of inoperable tumor with some degree of success. There are some tumors of grade 4 malignancy that are not satisfactorily attacked by either operation or radium therapy. Barringer has had only 1 patient with a tumor of grade 4 malignancy who remained well for eight years after treatment. Tumors of this grade should be irradiated externally before anything is done, after the specimen and the cystogram have been examined. If desired results are not obtained by external irradiation this should be supplemented by some form of internal irradiation. It is Barringer's belief that extensive tumors of grade 3 malignancy, difficult to remove or to irradiate, should be attacked by preliminary external irradiation. That method should be employed in the future, and, with careful application of external irradiation, it should add 5 per cent to the number of five-year cures.

Ferguson<sup>47</sup> reported that in 159 of 902 cases entered in the Bladder Tumor Registry, pneumocystograms were made. The procedure was said to be of value in the diagnosis of the lesion in 108 of these cases. A roentgen technic, favored in the treatment of carcinoma of the bladder, is the method of divided doses. Carcinoma of the bladder does not usually yield to a tissue dose of less than eight or ten erythema doses. If any such dose is to be delivered by external means of irradiation it must be by the technic of divided doses. This has been done successfully within the last eighteen months by Dean. The most satisfactory results seem to be obtained when it is known in advance that the malignancy of the tumor is either of grade 3 or grade 4. Carcinomas of grade 1 and grade 2, especially those that contain squamous pearls, are radio-resistant and do not yield to the average dose that can be delivered into the bladder in this manner.

Ferguson advocated ascertaining the possibilities of roentgen treatment of carcinoma of the bladder, making a biopsy in every instance, utilizing the Coutard technic or some modification of it in delivering tissue doses adequate to carcinomas of grades 3 and 4 and avoiding treatment by this method of tumors of grade 1 or 2.

*Urinary Incontinence*—Abeshouse<sup>48</sup> stated that incontinence of urine is an uncommon, although not an infrequent, complication of oper-

46 Barringer, B. S., in discussion on Pfahler and Vastine,<sup>45</sup> J. A. M. A. **104** 613 (Feb. 23) 1935.

47 Ferguson, R. S., in discussion on Pfahler and Vastine.<sup>45</sup>

48 Abeshouse, B. S. Repair of Urinary Incontinence Following Prostatectomy by Transplantation of the Gracilis Muscle. Report of Two Cases, J. Urol. **33** 28 (Jan.) 1935.



Rich<sup>56</sup> reported that in 292 consecutive postmortem examinations of men aged 50 or over who died of a wide variety of causes at the Johns Hopkins Hospital during the past three years, frank carcinoma of the prostate gland was observed in 41 cases (14 per cent) in the microscopic section taken as a routine at necropsy. Thorough examination of each gland undoubtedly would have disclosed a larger number of these tumors, many of which were so small that they were not seen macroscopically at necropsy. The report indicates, however, that carcinoma of the prostate gland occurs more frequently than is ordinarily supposed. In 65.8 per cent of these 41 cases the tumor was not recognized clinically, having been in most instances too small to have produced symptoms or to have attracted attention on physical examination. The most common site of the tumors was near the outer margins of the gland, and, even when they were only a few millimeters in size the tumors showed a tendency to invade the capsule.

Moore<sup>57</sup> reported preliminary conclusions concerning unrecognized carcinoma in 375 prostate glands and discussed the morphology in 52 cases of this disease. The clinical diagnosis was not made in all instances. There was no distant metastasis, and the disease was limited to one anatomic lobe of the gland. In the material on incidence an additional 11 cases of manifest carcinoma of the prostate gland are included, making a total of 63 cases of carcinoma occurring in the 375 prostate glands.

Moore's conclusions were that carcinoma of the prostate gland occurs more frequently with increasing age until 29 per cent of men who are examined at necropsy after having lived into the ninth decade have the lesion. The disease is intimately associated with senile atrophy, and the growth probably results from epithelial cells which have previously undergone atrophy. It is predominantly a lesion of the posterior lobe of the gland, but it may arise in any portion of it. Carcinoma and benign enlargement of the prostate gland are two distinct diseases which occur independently. Malignant degeneration rarely occurs in acini already hyperplastic and involved in benign enlargement. Perineural lymphatic invasion in the capsule of the prostate gland is one of the earliest changes in carcinoma, but invasion of the seminal vesicles and distant lymphatic invasion are late manifestations.

*Physiology*—Deming, Jenkins and van Wagenen<sup>58</sup> stated that atrophy of the true prostate gland has been demonstrated after castra-

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56 Rich, A. R. On the Frequency of Occurrence of Occult Carcinoma of the Prostate, *J Urol* **33** 215 (March) 1935.

57 Moore, R. A. The Morphology of Small Prostatic Carcinoma, *J Urol* **33** 224 (March) 1935.

58 Deming, C. L., Jenkins, R. H., and van Wagenen, Gertrude. Some Endocrinological Relationships of Prostatic Hypertrophy. Clinical and Experimental Studies, Preliminary Report, *J Urol* **33** 388 (April) 1935.

urinae muscle is atonic or when lesions of the spinal cord, either congenital or acquired, render the musculature of the bladder inactive. Other muscles, such as the pyramidalis muscle, levator ani muscle and abductor longus muscle have been used for sphincteric action, but they are not as satisfactory for transplantation as the gracilis muscle. Dispensing with the normal use of this muscle is not a detriment to the patient. The muscle has a long, slim belly and is readily approached. It has a double supply of nerves and blood. Its upper two-thirds is supplied by the obturator nerve, which comes from the direction of the origin of the muscle and lies in the direction of the desired transplantation, so that it can be turned upward without injury to the nerve and blood vessels. The sex of the patient is not important except that there is more difficulty in exposing the urethra of the male. Tunnelling of the tissues for a few centimeters near the urethra is preferable to complete incision. Either the right or left muscle may be used, however, it seems that a right-handed person probably would be more conscious of the use of the right gracilis muscle, and adaptation of the new use of the muscle would be accelerated.

*Perineal Drainage*—Illyes<sup>50</sup> uses perineal drainage after resection of the bladder, diverticulectomy, ureteral implantation or any operation on the bladder in which perivesical leakage or infection is likely to occur. This does not include transvesical prostatectomy, in which procedure, after the enucleation, Illyes swabs the prostatic cavity with 30 per cent solution of silver nitrate and then packs it.

A blunt forceps is pushed under the symphysis pubis, to either side of the midline, penetrates the triangular ligament and emerges in the anterior triangle of the perineum. The drainage tube is drawn upward into the pelvis. This is done in both male and female patients, and with care injury to important structures can be avoided.

Holding upward the concave side of the slightly bent blunt forceps, the surgeon feels the lower part of the symphysis pubis and perforates the pelvic fascia  $1\frac{1}{4}$  inch (3 cm) from the midline, near the lower edge of the pubic bone. He presses down the inner end of the instrument toward the abdominal cavity in order that this end may remain in a straight line as much as possible, directly under the pubic bone. Thus he avoids injuring the urethra as well as the pudendal artery and nerve. At the sharp angled union of the two sides of the pubic bone under the symphysis pubis and the ligamentum arcuatum, respectively, he finds the lamina intercruralis connecting the two sides of the acute angle, in which are arteries and veins running to the corpus cavernosum. This

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<sup>50</sup> Illyes, Goza. Perineal Drainage for Certain Bladder Operations, Brit J Urol 7 1 (March) 1935

but in further advanced conditions metastasis was widespread. There was an average delay of fourteen months between the onset of symptoms and the first visit to a physician. In addition, there was an average delay of twelve months between the first visit to a physician and the first examination at the Memorial Hospital for the Treatment of Cancer and Allied Diseases, making the average total delay more than two years.

Because there are several lesions which may resemble cancer of the penis the diagnosis should always be based on histologic examination. Seventy-six per cent of the patients had regional adenopathy at the first examination, of the involved glands 50 per cent were cancerous. Biopsy of aspirated material was performed as a check on physical examinations. Twenty-four per cent of the patients did not have inguinal adenopathy at their first examination. Since metastasis did not develop subsequently in any of these cases management of the primary tumors must have been efficient.

The prophylactic treatment of cancer of the penis consists in circumcising all male infants a few days after birth. When the primary tumor was superficial and no larger than 2 cm. in diameter treatment with the radon plaque was successful in all cases. When the primary lesion was larger and had penetrated deeper, amputation was performed 1.5 cm. proximal to any visible or palpable evidence of degeneration. Of 51 patients, 64.6 per cent treated by the aforementioned methods are free from disease. Forty patients with inguinal metastasis were treated by surgical removal with or without irradiation. Five per cent are now free from evidence of cancer. It is recommended that operation for inguinal metastasis be delayed until the primary tumor has been removed and infection in the nodes has subsided. No type of external irradiation used by Dean was of value in treating inguinal metastasis from cancer of the penis.

Wolbarst<sup>61</sup> stated that there is no authentic recorded case of cancer of the penis in a Jew ritually circumcised in early infancy. Almost every writer on the subject has made the same comment, but the importance of this fact is in making it a convincing argument as to the prophylactic value of circumcision in the campaign against cancer of the penis and cancer generally. There is still considerable opposition to infantile circumcision by otherwise progressive physicians, they seem to prefer to wait until an existing phimosis becomes troublesome before considering circumcision, and by that time the precancerous lesion may be, and often is, already present. To be effective completely as a prophylactic measure against cancer, circumcision must be performed in early infancy. The point is often made that the freedom of Jews and Mohammedans from cancer of the penis is attributable to racial immunity, but the

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<sup>61</sup> Wolbarst, A. L., in discussion on Dean<sup>60</sup>

## PROSTATE GLAND

*Obstruction*—Thompson<sup>53</sup> reported that 630 patients with obstruction by the prostate gland were treated by the transurethral method at the Mayo Clinic in 1934. This is an increase of 39.6 per cent over the number of patients having the same operation in the preceding year. Included in these 630 cases, in which a total of 696 transurethral resections of the prostate gland were performed, are 23 in which the patients had submitted to the same operation at the Mayo Clinic in former years. In 5 of these cases the original growth was malignant, and recurrence could be expected. In the other 18 cases, in which recurrence was not expected, it was necessary to remove 82 Gm of tissue, on the average, in order to relieve the symptoms, in 7 of these cases the total weight of the tissue removed at both operations exceeded 25 Gm. These patients, on their return, refused to undergo any procedure other than transurethral resection. Because of the increased risk and longer hospitalization, prostatectomy was not urged. In each case of recurrence the stay in the hospital required for resection of the gland was less than a week, and there were no fatal cases.

The average weight of tissue removed per case during the year was 11.6 Gm, in 73 cases the amount exceeded 25 Gm. The average period of hospitalization was shorter than in former years, 58.1 per cent of the patients stayed one week or less, an additional 28.9 per cent left in the second week, and only 13 per cent remained longer. The average period of hospitalization was eight and one-tenth days. The period of hospitalization for the group as a whole was shortened by reduction in the number of cases in which preliminary suprapubic cystostomy was performed, in 21 cases such an operation was performed at the clinic, and in 12 cases cystostomy had been performed elsewhere. Thus, in a total of 52 per cent of the group, as compared with 12.2 per cent in the two preceding years, preliminary suprapubic cystostomy was performed.

The painful complication of epididymitis has been almost entirely eliminated by strict attention to methods of drainage by urethral catheter rather than by routine vasectomy. The latter operation was performed in only 24.6 per cent of the cases. Epididymitis occurred in only 8 of the 630 cases studied in 1934—an incidence of 1.3 per cent. Litholapaxy was performed at the same time as resection in 28 cases, and in 7 others a tumor of the bladder was removed transurethrally at the time resection of the prostate gland was performed. There were only 2 deaths—a mortality rate of 0.3 per cent for the series of 630 cases.

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<sup>53</sup> Thompson, G. J. Transurethral Surgery in 1934, Proc. Staff Meet., Mayo Clin. 10:220 (April 3) 1935.

meatus, and to the extent that this lies behind the penoscrotal angle it will involve a hair-bearing area. The scrotal and preputial type is the fourth method, of which the Ombredanne operation is the most modern example. The posterior portion of the canal is constructed from tissue coming from the scrotum, as in the Bucknall operation. The anterior portion, to a varying extent, is made from the tissue of the redundant prepuce. In this operation the posterior portion of the canal in the penoscrotal type, and particularly in the perineal type, of course draws its inner layer from scrotal, and consequently hair-bearing, tissue.

The method of parallel flaps probably produces the best restoration of the canal. It employs tissue free from hair and of fine texture, particularly well suited to its changed environment. The formation of fistula has been a relatively common complication in this type, requiring further operation for its repair, but it can generally be avoided by adherence to the principles of plastic surgery. These involve the union of tissue on relatively broad surfaces and never union of the edge-to-edge type. They also require careful hemostasis and care in regard to a thoroughly adequate blood supply. However, the blood supply of flaps thus fashioned is better than that available in most of the other operations. It is the belief of the authors that at the hands of experienced surgeons the operation gives satisfactory results. The Bucknall operation was preferred by one of them for more than ten years. It has the advantage of being almost fool-proof, and with modest experience great certainty exists that a full length canal, free from fistula, will be obtained as the result of a two-stage operation. Owing to the growth of hair in these urethral flaps the procedure has been abandoned, as this complication is considered unavoidable and introduces an element of late unsatisfactory results.

Ombredanne reported a series of 392 cases in which his method was employed. Lyle reported 9 cases, all the patients were children, and they were not followed into adult life. The procedure does not require diversion of the urinary stream. It is apparently free from any marked risk of fistula and creates a urethra of full length and adequate caliber. It is subject to the objection inherent in the Bucknall type of operation, namely, the subsequent development of hair with formation of stone and urethral irritation attributable to the fact that some of the skin utilized for the urethra comes from a hair-bearing area. According to the experience of Cabot, Walters and Counseller the operation is free from unusual technical difficulties, and it does create a satisfactory urethra without important danger of the formation of fistula.

*Absence of the Penis*—Drury and Schwarzell<sup>63</sup> reported a case of congenital absence of the penis of a boy aged 13.

<sup>63</sup> Drury, R. B., and Schwarzell, H. H. Congenital Absence of Penis, *Arch Surg* 30 236 (Feb.) 1935.

suggestion of carcinoma remains gold-screened radon perineal needles are used. Implantation of gold seeds through the perineum is ineffective because the gold seeds cannot be implanted with any degree of accuracy. After the patient has recovered from the foregoing procedure external irradiation should be given. The third class consists of cases in which the prostatic carcinoma is so enormous that it seems impossible to control. External irradiation alone is given, and if urinary retention is a dominant symptom transurethral resection should be performed. The fourth class contains cases in which there is metastasis to bone or metastasis around nerves in which amelioration is to be expected. In these cases external irradiation alone should be used. It is surprising how many years the lives of patients with metastasis to bone can be prolonged by this method.

Graves and Miltzer<sup>55</sup> presented a clinical review of 81 cases of carcinoma of the prostate gland with metastasis and made a preliminary report of a pathologic study of the paths of dissemination in cases of this disease. In all but 6 cases of the entire series, metastasis to bone was found either by roentgen examination or at necropsy. The pelvis and sacrum were involved in 85 per cent of the cases, and the lumbar part of the spinal column was affected in 59 per cent. Pathologic fractures were observed in 5 instances.

Treatment of the local condition was necessarily limited to measures of palliation. The plan of treatment in cases of carcinoma of the prostate gland with metastasis cannot be standardized, and the procedure adopted in each case must vary with the needs of the individual patient. Transurethral resection sometimes forestalls the need for more extensive operation. High voltage roentgen irradiation and radium therapy proved to be the most effective agents for the relief of pain caused by metastasis.

Postmortem examinations were made on 74 per cent of the patients who died in the hospital. Metastasis other than in the bone was found most frequently in lymph nodes, in the lungs and in the liver. Pyelonephritis was the direct cause, or the most important contributing cause, of death in 41 per cent of the cases. It was observed clinically that advanced renal infection may exist without significant pain and tenderness in the region of the kidney. Extensive pyelonephritis may be present without marked elevation of the nitrogen content of the blood. The test of renal function with phenolsulphonphthalein frequently affords a more accurate picture of the degree of damage to the kidney than do chemical examinations of the blood.

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<sup>55</sup> Graves, R. C., and Miltzer, R. E. Carcinoma of the Prostate with Metastases, *J. Urol.* **33** 235 (March) 1935.

were good, in 5 cases, in all of which the testes had been intra-abdominal at operation and in which in order to accomplish the Torek procedure extreme traction on the vessels had been necessary, the results were only fair. In 2 cases, orchidectomy had become necessary, and in 7 cases no adequate check on results was obtained.

Cabot<sup>65</sup> discussed three methods available at present for treating cryptorchidism. The first method is to let nature take its course, in which event it is certain that in a considerable proportion of the cases no alteration in the abnormal position of the testis will take place and permanent damage to the testis will occur. Regarding the second method, recent experimental evidence suggests that the use of a hormone derived from the anterior lobe of the pituitary gland markedly affects the development of the genital apparatus and stimulates descent of the abnormally placed testis into the scrotum. The number of instances in which this treatment has been applied to children is not sufficient to warrant a conclusion, and the method should be regarded as being still in the experimental stage. It should be emphasized, however, that this method should not be used to the detriment of the child and that its use should preferably be confined to the period between 3 and 8 or 9 years of age. If the testis has not descended into its normal position by the end of that period the method should be abandoned and operation resorted to. In the third procedure for undescended testis the work of Moore modified the views in regard to what constituted a satisfactory operative result in that it required the placing of the testis in an entirely normal position and maintaining it there. This increased the importance of the Torek type of operation as compared with other methods. Operations of the Bevan type do not so consistently fulfil this indication completely and should, according to Cabot, be largely abandoned. In regard to patients with intra-abdominal cryptorchidism, in the treatment of whom the technical difficulties of obtaining normal replacement are great, Cabot's experience indicates that a two-stage operation, in which the testis is brought down to below the level of the external inguinal ring in the first stage and to a normal position in the second stage, by the application of the Torek technic, is likely to be satisfactory in many cases.

#### URINARY CALCULI

*Experimental Studies*—Higgins<sup>66</sup> reported that in a high proportion of albino rats maintained on a diet deficient in vitamin A, calculi of the urinary tract developed. If deficiency in the diet was

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<sup>65</sup> Cabot, Hugh, in discussion on Thiessen and Walters<sup>64</sup>

<sup>66</sup> Higgins, C. C. Production and Solution of Urinary Calculi. Experimental and Clinical Studies, J. A. M. A. 104: 1296 (April 13) 1935.

tion There is no evidence that castration causes atrophy of the so-called benign overgrowth of the prostate gland The anatomic origin of prostatic hypertrophy has been definitely established Studies have disclosed absence of submucosal glands of the prostatic urethra and trigon in the monkey, hence there is less probability of the development of prostatic hypertrophy in this animal The rat has all the anatomic structures that might serve as origins for hypertrophy of the prostate gland A case in which hypertrophy of this gland developed from the submucosal glands of the posterior urethra of an old rat is reported

*Stone*—Thompson and Cook<sup>59</sup> stated that chronic prostatitis often persists because of infected pockets or diverticula that drain only through a small prostatic duct Treatment by ordinary methods, such as massage, irrigation, injection of antiseptic substances or diathermy, results only in temporary relief of symptoms Surgical treatment of these structures by the transurethral route insures adequate drainage and subsequent improvement in a large percentage of cases The cavities of the prostate gland must be widely excavated in the form of a saucer, and, if necessary, tissue must be excised to provide free flushing at the time of urination, otherwise infection will persist Calculi embedded in the tissue of the prostate gland, which occur either primarily or secondarily to infection, can be removed by transurethral operation

#### PENIS

*Epithelioma*—Dean<sup>60</sup> presented a clinical study of 120 cases of epithelioma of the penis in which radium and roentgen therapy were used and considered the review significant in view of the fact that sufficient time had elapsed to determine to a fair degree the value of these agents Married men predominated in this series in the ratio of 5:1 Occupation and previous constitutional diseases (excluding syphilis) seemed to be of no etiologic importance Thirty-four per cent of 70 patients had had syphilis, and the syphilitic patients, as a group, were 8 years younger than the nonsyphilitic patients when the symptoms of cancer appeared No Jews were found in the series Only 4 per cent of 93 patients had a freely retractile prepuce At least 65 per cent had some mechanical difficulty in retracting the prepuce Thirty-seven per cent of the patients had been operated on to expose the glans penis The flat type of cancer of the penis occurred more frequently than the papillary type The two types seem to grow at the same rate, but the flat tumors metastasize earlier The inguinal nodes were the site of the earliest metastasis,

59 Thompson, G. J., and Cook, E. N. Chronic Prostatitis and Prostatic Calculus. Treatment by Incision with the Electrocautery, *J. A. M. A.* **104**:805 (March) 1935

60 Dean, A. L., Jr. Epithelioma of the Penis, *J. Urol.* **33**:252 (March) 1935



In the remaining rats in this series the calculi were definitely smaller. In one the renal calculi also had disappeared. Cystitis, hemorrhage under the mucosa of the bladder, and renal infection were commonly observed in this group. Keratinization of the epithelium was present to some degree in the genito-urinary tracts of all the animals in this series. A reparative process was evident in the epithelium of the ureters, kidneys and bladder, especially when there was not a marked degree of infection.

These experiments show that with the addition of vitamin A to the diet there is a tendency toward restoration of the normal epithelium along with solution of the calculi. In the first experiments at the Cleveland Clinic the calculi produced in rats on a diet deficient in vitamin A were composed chiefly of calcium phosphate, hence it seems logical to assume that the calculi in this series of experiments were of the same composition. An acid ash diet high in vitamins, especially in vitamin A, is suggested as a prophylactic measure to prevent the recurrence of calculi in patients who have had urinary lithiasis, and the rôle of vitamin A in the diet to prevent primary calculous disease is important. A high vitamin, acid ash diet has produced decrease in the size of, or total disappearance of, renal calculi in patients refusing surgical intervention and in those in whom operation has not seemed indicated. In 18 collected cases in which the high vitamin, acid ash diet has been used the renal calculi have undergone solution, according to roentgenographic evidence.

*Spontaneous Fragmentation* —Chauvin<sup>67</sup> stated that the spontaneous fragmentation of calculi within the kidney, urinary ducts and bladder, although well known from ancient times in its anatomic modalities, remains as much a mystery as ever in its pathogenic mechanism. Various theories have been proposed, the oldest on record is that of Civiale, who thought that the stones were broken by contractions of the bladder. Other writers have ascribed the fragmentation to progressive desiccation of the stone from the center to the periphery, to the progressive increase in size of the nucleus from imbibition, which was supposed to have shattered the cortex, and to the action of mineral waters. None of these explanations is entirely satisfactory, and some are actually fantastic.

To understand how certain concretions break diametrically through their entire mass it is necessary to assume that a change occurs in the size of the whole stone, both nucleus and cortex, and such a change can be explained only by a modification of the chemical composition of the stone. The calculus is constantly bathed with urine, now, the reaction and composition of this urine may change, and there is nothing to

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<sup>67</sup> Chauvin, E. La fragmentation spontanée des calculs urinaires, Arch d mal d reins 8 53 (Jan) 1934.

inherent weakness of this contention has been shown by the work of Sorsby and others and also by the case of cancer in an uncircumcised Jew which Wolbaist reported in 1932. So far as can be ascertained, this is the only reported instance of cancer of the penis in a Jew. If he had been born with racial immunity it must have become seriously attenuated by virtue of his retained foreskin.

*Hypospadia*—Cabot, Walters and Counseller<sup>62</sup> reported on 38 cases of hypospadia in which operation was performed between May 1, 1930 and May 1, 1934. Besides the various procedures directed toward correction of the deformity, three general methods of constructing a urethra were principally used: the lateral flap method, a development of the old principles of Duplay and Thiersch (26 cases), the Bucknall method and the Ombredanne method. The operations should be divided into two groups, those concerned with correction of the deformity of curvature and those concerned with construction of the urethra. Procedures intended to overcome the deformity of curvature should be undertaken at an early age, preferably between 1 and 2 years. The smallness of the parts is not considered a handicap to this phase of the operation. The optimal time for building of the urethra is after the child has attained reasonable growth and yet some years before puberty. This procedure is best undertaken some time in the sixth year, three or four years after the deformity has been corrected. In most of the methods employed diversion of the urinary stream will be desirable. This is not necessary in the Ombredanne operation but is essential in operations of the modified Duplay and Thiersch type. In the experience of Cabot, Walters and Counseller drainage through a perineal boutonniere made at the completion of the operation of repair has been satisfactory.

At present operations for hypospadia involve four types of procedure. There is the parallel flat type in which the urethra is made by turning in flaps with broad bases cut parallel to the normal course of the urethra and so planned as to avoid superimposition of the suture lines in the two layers. All modifications of this type are from the principles originally enunciated by Duplay and by Thiersch. It is significant that the flaps utilized in this procedure contain no hair-bearing skin in any portion. The second type involves the principle of the pedicle flap, these flaps being taken from more or less distant regions and manipulated at various stages of the procedure so as to construct a urethra. This method has been used with skill by Blain and others. In the third type, scrotal flaps are used. The typical procedure of this group is the Bucknall operation. The inner layer of the urethra is formed from the tissue extending backward from the abnormally placed

<sup>62</sup> Cabot, Hugh, Walters, Waltman, and Counseller, V. S. Principles of Treatment of Hypspadias, *J Urol* 33 400 (April) 1935.

## CAUSES OF DEATH AFTER OPERATIONS ON THE URINARY TRACT

Hyman and Mencher<sup>68</sup> reported a study of the causes of death after operations on the urinary tract, reviewing 168 cases with 119 postmortem examinations

There were 27 cases of renal calculus. The causes of death were infection of the wound in 1 case, pyelonephritis in 12, peritonitis in 3, postoperative shock in 2, cardiac failure in 1, sepsis in 3, hemorrhage in 2, cerebral accident in 1, obstruction of the upper portion of the intestinal tract in 1 and general debility with decubitus and tabes in 1. In 11 of these 27 cases a bilateral involvement was found, in 9 cases the calculus was associated with pyonephrosis, in 3 solitary kidneys were present, and in 4 the patients were admitted in a state of uremia.

In the fifteen cases of tumor of the kidney the causes of death were infection of the wound in 2 cases, pneumonia in 1, peritonitis in 1, shock in 3, pulmonary embolism in 2, hemorrhage in 3 and advanced carcinoma in 2. In 1 case death followed spinal anesthesia. One of the tumors was infected. In 11 cases nephrectomy was performed, and in 4 the surgical intervention was limited to exploratory operations, no further procedure being available. In 4 cases nephrectomy was performed by the transperitoneal route.

In 5 cases of renal tuberculosis death resulted from the following causes: renal infection in 1 case, tuberculous meningitis in 1, pulmonary embolism in 1, generalized tuberculosis in 1 and solitary kidney with advanced tuberculosis in 1. Two of these 5 patients were admitted in a state of uremia, 1 had bilateral tuberculosis, 2 had associated pyonephrosis, and 1 had calculus pyonephrosis. Two patients underwent nephrectomy, 2 nephrostomy, and 1, a transplantation of the ureter to the skin. In this group the disease itself was the prime cause of death.

In 10 cases of pyonephrosis death was attributable to the following causes: pulmonary embolism in 1 case, renal infection (original disease) in 5, sepsis in 3 and chronic glomerular nephritis in 1. Four patients were admitted in a state of uremia, and 1 entered with sepsis.

There were 10 cases of perinephric abscess, suppurative pyelonephritis and cortical abscess. The causes of death were as follows: peritonitis in 1 case, shock in 1, infection of the wound in 1, pulmonary embolism in 1, sepsis in 3 and renal infection in 3. Four of these patients were admitted in a state of uremia, and 2 with sepsis. In 2 cases nephrectomy was performed, in 5 only incision and drainage comprised the procedure, and in 3 nephrostomy was performed.

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68 Hyman, A., and Mencher, W. H. The Causes of Death After Urological Operations. A Study Based on One Hundred and Sixty-Eight Cases with One Hundred and Nineteen Autopsies, *J Urol* 33 315 (March) 1935.

There were no subjective symptoms, and the patient's physical and mental development were those of the average boy of his age. The testes, spermatic funiculi and vasa deferentia were normal. Urine was discharged from the rectum three or four times a day. Although excretory urography gave evidence of a bilateral hydro-ureter and some pelvic dilatation there were no symptoms of urinary infection.

This condition is extremely rare. In the 7 cases previously recorded accompanying congenital defects were common, and ectopic erectile tissue was frequently noted. This patient had no other demonstrable abnormalities. This is the first case reported in which the urinary tract has been visualized by roentgenograms.

#### TESTIS

*Cryptorchidism*—Thiessen and Walters<sup>64</sup> reported on 96 cases of undescended testis in 72 patients operated on at the Mayo Clinic, in which treatment was by temporary fixation of the testes to the thigh. The Torek method of operation was used in all these cases, and satisfactory results were obtained in 92 per cent of them. In 73.9 per cent of the cases an indirect inguinal hernia, which was associated with the undescended testis, was repaired surgically at the same time. In 47.2 per cent of the cases cryptorchidism was bilateral. Of cases in which there was unilateral nondescent of the testis the right side was affected in almost three times as many instances as the left side. The right testis was undescended in 38.8 per cent, and the left testis, in 13.8 per cent of the cases. The positions of these testes were classified into four groups. The 18 (18.7 per cent) testes in the first group were found at operation to be intra-abdominal. In the second group were 3 (3.1 per cent) testes situated at the internal inguinal ring, in the third group, 40 (41.7 per cent) testes lying in the inguinal canal, and in the fourth group, 35 (36.5 per cent) testes which were situated at the external inguinal ring.

The results of the operations have been satisfactory. Seventy-six (79.1 per cent) of the testes were maintained in normal position in a scrotum of normal size. The size of 32 (33.3 per cent) of the testes increased after operation. Eight (8.3 per cent) of the testes which before operation had been small or atrophic remained in that condition. After operation the testis was found to be in the upper portion of the scrotum in 16 cases, but before operation in 10 of these 16 cases the testis had been within the abdomen. In 69 (77 per cent) of the cases results were excellent, in 13 (14.6 per cent) results apparently

<sup>64</sup> Thiessen, N. W., and Walters, Waltman. Cryptorchidism, Proc. Staff Meet., Mayo Clin. 10: 132 (Feb. 27) 1935.

in which prostatectomy was performed in two stages, death resulted from the following causes. Infection of a kidney in 1 case, pulmonary embolus in 1 and sepsis in 1. In this group of operations on the prostate gland the general condition of the patient is important. Most of these patients are in the sixth or seventh decade of life and have, in addition to the prostatic disorder, coronary disease, myocarditis, generalized atherosclerosis or diabetes. Whereas in 45 per cent of the cases infection in one form or another was the important factor in the cause of death, the cardiovascular system and pneumonia accounted for an equal number of deaths. It is interesting to note that 15 patients died after undergoing ordinary suprapubic cystotomy. In a review of 294 cases of cystotomy and completed suprapubic prostatectomy, the mortality rate proved to be as follows: cystotomy only, 17 cases with 8 deaths, suprapubic prostatectomy in one stage, 44 cases with 3 deaths, suprapubic prostatectomy in two stages, 233 cases with 20 deaths. Although 11 patients died in an apparent state of uremia, the underlying factor was severe infection of the kidneys.

Primary causes of death in the entire series studied by Hyman and Mencher were as follows: renal infection in 45 cases, sepsis in 23, infection of the wound in 12, pneumonia in 11, peritonitis in 11, shock in 11, cardiovascular disease in 10, pulmonary embolus in 9, hemorrhage in 7 and cerebral conditions in 3—a total of 142 deaths. Contributing factors were these: uremia in 64 cases, renal infection in 19, sepsis in 2, infection of the wound in 17, pneumonia in 12, peritonitis in 6, shock in 3, cardiovascular disease in 4, pulmonary embolus in 3, hemorrhage in 3 and cerebral conditions in 1. Certain facts are emphasized by this study. There are complications which are unavoidable despite careful preoperative preparation, technical skill and assiduous postoperative care. Among these may be mentioned pneumonia, cardiovascular disease, cerebral factors and pulmonary embolism. Infection of the wound, to a certain extent, can be controlled. Excessive suturing of wounds in the presence of gross infection is to be avoided. Free drainage and protection of the perivesical and retrovesical region in all operations on the bladder is of prime importance. The necessity of protecting the peritoneum and immediately suturing all rents in that lining cannot be too strongly emphasized. Careful aseptic technic is essential to prevent introduction of infection during the irrigation of an organ through urethral and ureteral catheters and through suprapubic tubes or those used in nephrostomy. Control of hemostasis is obviously necessary. Another point to be taken into consideration is avoidance of excessive fulguration and irradiation of infected organs. Needless pyelographic and instrumental examinations should be avoided as much as possible, especially in cases of infection.

continued for two hundred and fifty days, 85 per cent of the experimental animals exhibited calculi of the bladder, and 42 per cent, calculi of the kidney. The spherical, light brown stones varied from 0.5 to 8 mm in diameter. They contained calcium phosphate chiefly, with traces of carbonates and a small amount of mucoid substance. No uric acid or oxalates were detected.

Three constant changes observed in these animals, that might be associated with formation of stones, were keratinization of the epithelium of the genito-urinary tract, urinary infection and alkalimuria. The keratinization of the epithelium was noted after the diet had been deficient in vitamin A for a period of from eight to ten weeks. Urinary infection was produced in a large percentage of rats maintained for long periods on a diet deficient in vitamin A. Infection of the bladder occurred usually after thirty days, and renal infection, after from sixty to ninety days. When the experiments had progressed for from two hundred to two hundred and fifty days 72 per cent of the rats had infection of the bladder, and in 42 per cent of these animals there was a coexistent renal infection. Alkalimuria was a constant finding in rats maintained on a diet inadequate in vitamin A. By the addition of ammonium chloride to the diet the incidence of calculi was decreased. When vitamin A was added to the deficient diet the urine became acid and calculi were not produced.

It was demonstrated in earlier experiments that if vitamin A alone was restored to the diet of rats the formation of urinary calculi could be prevented. In order to determine whether stones already formed could be dissolved by the administration of vitamin A, 30 rats with calculi of the bladder or kidney were studied. Except for the addition of cod liver oil, the diet was the same as that given when the stones were produced. Twelve rats with calculi of the bladder received the deficient diet for from thirty to sixty days. In 11 of these the calculi had entirely disappeared, as evidenced by roentgenograms, after 2 drops of cod liver oil had been given daily for a period of from fifty to sixty days. In a second group of 11 rats which had received the deficient diet for from ninety-six to one hundred and thirty days calculi of the bladder could be demonstrated roentgenographically, and coexistent renal calculi were observed in 2 rats. After the rats had been on the diet high in vitamin A for ninety days, roentgenograms gave no evidence of calculi in the bladders of 6 rats. In the other 5 the calculi were definitely smaller. The third group of 12 rats had been maintained on the deficient diet for one hundred and eighty days. Vesical calculi had been demonstrated in all these rats, and renal calculi were present in 2 of them. In four animals the calculi of the bladder had entirely disappeared one hundred and one days after cod liver oil had been added to the diet.

cooperate more closely to explain many obscure clinical pictures of abdominal distress which are the referred symptoms of primary urologic disease

Brooks,<sup>71</sup> in discussing the gastro-intestinal manifestations of urologic disease, stated that nausea and vomiting are the most outstanding signs of renal disease. Pyelitis, renal stones, renal abscess or small cortical abscesses often cause these gastro-intestinal disturbances without markedly localizing symptoms pointing to the urinary tract as the affected part.

McKenna<sup>72</sup> stressed the frequency with which seminal vesiculitis causes referred pain at McBurney's point. Friedenwald emphasized the fact that stone in the pelvis of the kidney often produces symptoms resembling duodenal ulcer or cholecystitis, giving rise to pain several hours after meals, with signs of hyperacidity, or with reflex and colicky pain in the upper part of the abdomen. The true condition may remain obscure unless a thorough investigation is made. In a number of instances in which the patient previously had been under treatment for a considerable time for a supposed gastric cancer, subsequent examination indicated toxemia secondary to hypertrophy of the prostate gland as the cause of the nausea, vomiting and abdominal pain.

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71 Brooks, Harlow, in discussion on Portis and Grove.<sup>70</sup>

72 McKenna, C. M., in discussion on Portis and Grove.<sup>70</sup>

prevent a calculus that was, for instance, originally of uric acid, from becoming a uratic stone if the urine becomes alkaline, this would cause a change in size, not of the nucleus or of the cortex, but of the whole mass of the concretion, and would necessarily fissure the latter through and through

If the nucleus and cortex have not the same chemical composition, only one of the constituents may undergo chemical modification, and the fissuration may then involve only one. It is more difficult to explain why certain calculi break in irregular lines while others exhibit geometric regularity in their lines of cleavage. But when one considers the fragments of the latter one is led to see a resemblance with the mode of cleavage of certain crystals and to ask whether the amorphous or the crystalline structure of the salts composing any given stone does not explain the particular type of fragmentation of the one or of the other variety of stone. It is possible that crystallographic examination of these stones would solve this problem.

The stones that have been the least studied with reference to their fragmentation are those that occur within the kidney. These calculi, often coralliform, are phosphatic, and it is easy to understand how the least violence would cause them to rupture. Stones forming in the ureter or urethra lengthen as they grow, changing from the shape of the pit of an olive to that of a pit of a date and finally to a rodlike shape, through apposition of successive layers at the posterior or central extremity. When they are sufficiently developed they easily break along the lines of least resistance, by cleavage of the strata that have been deposited. Stones in the urethra are poorly protected, and it is not surprising that they break under trauma. The fragments then often become articulated so that they are termed articulated calculi. Vesical calculi show several kinds of fragmentation: (*a*) by cleavage, (*b*) by cracking and (*c*) by a combination of cleavage and cracking. The cracking may occur without any system of regularity or it may take place along lines of radiation oriented toward the center. According to some authors these radii start from the center, and when they reach the surface the fragments fall apart, dividing the calculus into regular halves, quarters and so forth. Chauvin found it possible in one case to produce the same type of regular cleavage by crushing whole stones in his hand. In the third type the cortex first separates from the nucleus, then these lines of radiation develop in the former while the nucleus remains entire. This type of fragmentation is seen most frequently in uric acid stones, and especially in hollow ones in which the nucleus has been resorbed. Oxalic calculi, the structure of which is, as a rule, regular and homogeneous, never undergo fragmentation.



Southern Minnesota Medical Association and an honorary and corresponding member of several foreign societies

During the World War he was active as a teacher in the school for developing surgeons which was established at the Mayo Clinic, and from time to time since he has taken part in work designed to give those continuing in the medical corps of the United States Army a more intimate knowledge of diagnostic and operative procedures



E STARR JUDD

1878-1935

In 1921 Dr. Judd was made a member of the editorial board of the ARCHIVES OF SURGERY. His opinions have always been sought in determining the policy of this publication. He had a stabilizing influence such as few possessed. Simple, almost shy, he was possessed of great wisdom, he could settle discussion by kind reason. He will be deeply missed by all who learned by association with him to know his greatness. His memory will be kept alive by the works which he has produced.

In the group of 72 deaths following operative procedures on the kidney for various conditions death was attributable to infection of some type in 40 cases (56.3 per cent). At least 30 patients died with uremic manifestations, 16 of them entering the hospital in a state of uremia. The principal factor in the causation of the uremia was infection.

There were 4 cases of calculus of the ureter, in these death was caused by infection of the wound in 1 case and by renal infection, cardiac disease and sepsis, respectively, in the other cases.

The causes of death in 25 cases of tumor of the bladder were as follows: infection of the wound plus other causes in 6 cases, pneumonia in 1, renal infection in 3, peritonitis in 2, shock in 2, cardiovascular disease in 2, pulmonary embolus in 1, sepsis in 4, undetermined cause in 2, thrombosis and gangrene involving the iliac artery in 1 and paralytic ileus in 1. In 5 cases of contracture of the neck of the bladder death was attributable to the following causes: peritonitis in 1 case, shock in 1, sepsis in 1 and renal infection in 2. All the patients in this group underwent suprapubic operations. The case of peritonitis was not attributable to any operative procedure but to rupture of an abscess of the spleen. Renal infection in 1 instance and pulmonary embolus in the other were the causes of death in the 2 cases of diverticulum of the bladder. In 2 cases of exstrophy of the bladder in 2 young children in whom the ureter was transplanted to the bowel death was caused by pneumonia in 1 and by intestinal obstruction at the site of implantation of the ureter in the other. The cause of death in all 4 cases of stone of the bladder was renal infection. In this group of 39 deaths following operation on the bladder, 25 patients (more than 64 per cent) died as a result of infection originating in the wound or in the urinary tract. The mortality from infection in the group of patients who had tumors was unusually high. The remaining causes of death are fairly evenly distributed among other complications.

There were 15 cases of adenoma of the prostate gland in which the first stage of suprapubic cystotomy was performed. The causes of death were as follows: pneumonia in 4 cases, infected kidney in 4, cardiac disease in 3, pulmonary embolus in 1, sepsis in 1, hemorrhage in 1 and phlegmonous colitis in 1. Six of these patients were admitted with acute urinary retention, 2 had vesical calculi, and 2 were admitted in a state of uremia. The causes of death in 13 cases of adenoma of the prostate gland, in which prostatectomy was performed in two stages, were as follows: infection of the wound in 1 case, pneumonia in 2, infection of a kidney in 3, cardiac disease in 2, sepsis in 2, hemorrhage in 1, diabetic acidosis in 1 and meningitis in 1. In 3 cases of adenoma

the air may be withdrawn in part following ventriculography is urged by some workers as a reason to prefer this method over encephalography

A more dangerous result of the injection of air is intracranial hypertension, even though the pressure may have been subnormal at the end of the injection Tschugunoff<sup>4</sup> noted increased pressure following the injection of air in 82 per cent of 32 cases which he studied Whether the injection of air stimulates an increased production of cerebrospinal fluid or impairs its absorption is not clear However this may be, when a condition of intracranial hypertension already advanced is exaggerated by this mechanism, the procedure may become a real danger, and fatalities have been attributed to this cause<sup>5</sup>

There can be little doubt that air is an irritant to the central nervous system Although the initial acute reaction might conceivably be explained as the result of an alteration of pressure incident to the withdrawal of spinal fluid and the injection of air, the less intense and more prolonged reaction, as well as the subsequent increase of intracranial pressure, seems better explained on an irritative basis Cytologic studies on spinal fluid and experimental studies on the pathologic changes<sup>6</sup> following the injection of air corroborates this opinion, and one may conclude with Eley and Vogt "Obviously a temporary sterile meningitis is established by the irritative effect of the air"

It may be concluded, then, that although the injection of air has proved to be an essentially safe procedure it nevertheless remains a painful and trying ordeal for the patient, usually requiring the use of an anesthetic and four or five days' hospitalization Its safety, too, is not unqualified, it depends on a careful selection of cases and a development of technic These very factors limit its application and scope of usefulness

#### REVIEW OF THE LITERATURE

Such factors have led various workers to seek other methods of encephaloventriculography These methods have been chiefly of two general types—the use of opaque fluids and the use of gases Judging from the literature the first of these experimental methods has received most attention

4 Tschugunoff, S A Zur Frage uber die Veranderungen der cerebrospinalen Flussigkeit nach der Encephalographie, *Ztschr f d ges Neurol u Psychiat* **122** 452, 1929

5 Grant, F C Surgery of the Head, Spinal Cord and Peripheral Nerves, *Progressive Med* **1** 48 (March) 1930 Adson, A W Evaluation of Pneumoventriculography and Encephalography, *Am J Roentgenol* **27** 657 (May) 1932

6 Eley, R C, and Vogt, E Encephalography in Children, Further Observations in Children with Fixed Lesions of Brain, *Am J Roentgenol* **27** 686 (May) 1932 Jacobi, W Zur Frage der Spatschadigungen nach Encephalographie, *Deutsche Ztschr f Nervenhe* **112** 266, 1930 Tschugunoff<sup>4</sup>

Braasch,<sup>69</sup> in discussing the causes of death after operations on the urinary tract expressed the belief that many of the deaths that resulted from infection following surgical procedures on the lower part of the urinary tract, such as prostatectomy and resection for tumor of the bladder, were caused by inadequate technic in drainage. Another cause of death is pulmonary embolism. This complication follows operations on the perineum, on the female pelvis and on the region of the prostate gland more frequently than operations on other regions. It is of interest to note that pulmonary embolism was observed in only 1 of approximately 1,000 cases of transurethral resections for obstruction by the prostate gland. It has been the experience of the Mayo Clinic that some of the newer substances employed for local and spinal anesthesia, and described as being harmless, have proved to be exceedingly toxic in some cases. Braasch mentioned a nonoperative death which resulted from the use of one of the newer "harmless" substitutes for cocaine, which was injected into the urethra. Death occurred instantaneously when injection was made into the urethra twenty-four hours after an attempt had been made to dilate a stricture. It is advisable to employ in the urethra after trauma only local anesthetics that are known to be innocuous. Renal insufficiency is undoubtedly an occasional cause of death. The various tests of renal function made prior to operation may give results that are normal or nearly so. In case of bilateral nephrolithiasis and stone in a solitary kidney, an elevated urea content of the blood of from 40 to 50 mg per hundred cubic centimeters would not necessarily indicate renal insufficiency. However in such cases, even after a simple operation, renal insufficiency occasionally develops, and death has occurred.

#### GASTRO-INTESTINAL MANIFESTATIONS OF UROLOGIC DISEASE

Portis and Grove<sup>70</sup> concluded, from a study of various obscure gastro-intestinal disorders, that urologic diseases are frequently the causes of referred symptoms. They suggested that the interrelationship of the nerve paths of the urinary and gastro-intestinal tracts may explain this curious relationship of symptoms. Women in whose urethras pathologic changes have taken place frequently show gastro-intestinal manifestations. Pressure phenomena and displacement are factors in a certain group of cases. Pathologic changes in the lower part of the urinary tract in male patients may cause symptoms, particularly in middle-aged patients. The gastro-enterologist and urologist should

<sup>69</sup> Braasch, W. F. in discussion on Hyman and Mencher.<sup>68</sup>

<sup>70</sup> Portis, S. A., and Grove, J. S. The Gastro-Intestinal Manifestations of Urologic Disease. *J. A. M. A.* 104:710 (March 2) 1935.

In two instances the iodized poppy-seed oil 40 per cent penetrated to the brain and caused a local glial reaction and formation of cysts. Bruskin and Propper tried to explain the reaction in terms of mechanical and chemical irritation, the latter resulting from a slow splitting down of iodized poppy-seed oil 40 per cent to iodine and its products of saponification.

Putnam<sup>21</sup> in 1926 reported the use of brominized oils in radiography. He found that brominized lard was the most suitable of the oils tested and that it was less irritating to the tissues than air.

In 1928 Frazier and Glasser<sup>22</sup> reported the experimental use of iodized rape-seed oil intraventricularly, without conclusive results.

Skiodan was used by Lindstrom and by Arnell<sup>23</sup> but was found to be unsuitable.

Iodized poppy-seed oil was used by Pieper and Klose<sup>24</sup> and Bruskin and Propper. It proved to be toxic, except in small amounts. They also found that it produced definite pathologic changes in the central nervous system, regardless of the amount used.

In 1932 Radovici and Meller<sup>25</sup> reported the use of a preparation of thorium dioxide. Even small amounts caused an elevation of temperature. Evidently the meninges and central nervous system are not indifferent to this substance.

In general, it appears that opaque fluids are nontoxic and inert so far as they are insoluble and stable. Even then, mechanical irritation and a foreign body reaction may be produced in the central nervous system. Furthermore, the necessarily limited amounts which may be injected make this method rather inadequate from the standpoint of demonstrating the general ventricular outline.

Although gases, on the other hand, permit of roentgenograms of more limited contrast, they appear to be better tolerated and to permit a more complete filling and study of the ventricular and subarachnoid spaces and are absorbed with relative rapidity. There seems to have been little work done on gases other than air.

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21 Putnam, T. J. Brominized Oils for Radiographic Use. Preliminary Report, *J. A. M. A.* **87** 1102 (Oct. 2) 1926.

22 Frazier, C., and Glasser, M. A. Iodized Rape-Seed Oil (Campidol) for Cerebrospinal Visualization, *J. A. M. A.* **91** 1609 (Nov. 24) 1928.

23 Arnell, S. Encephalography with Solution of Contrast-Salt, *Acta radiol.* **13** 43, 1932.

24 Pieper and Klose, cited by Bruskin and Propper<sup>20</sup>.

25 Radovici, A., and Meller, O. Encephalographie liquidienne par le thorotrast sous-arachnoïdien, *Rev. neurol.* **1** 479 (March) 1932, *Essai de liquidographie cephalo-rachidienne, encephalo-myelographie par le thorotrast sous-arachnoïdien*, *Bull. Acad. de med., Paris* **107** 314 (March 1) 1932.

## Obituaries

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E STARR JUDD

1878-1935

Dr E Starr Judd passed away on Nov 29, 1935, after a short illness. Death was caused by pneumonia. In his death surgery has lost one of its outstanding exponents. Possessed of rare surgical judgment, keen diagnostic sense and rare technical ability, he exhibited all the qualities of a master surgeon. He was born in Rochester, Minn., on July 11, 1878, and was graduated from the University of Minnesota School of Medicine in 1902. After serving an internship in St. Mary's Hospital at Rochester, he became an assistant of Dr. C. H. Mayo in 1903.

He successively passed through the grades of the hospital and medical school staffs and at the time of his death was surgeon to St. Mary's Hospital, professor of surgery in the graduate school of the University of Minnesota and head of a section in the division of surgery at the Mayo Clinic.

Early in his professional career he became interested in organized medicine. He served as president of the Minnesota State Medical Association and was secretary of the Section on Surgery of the American Medical Association in 1913-1916 and chairman of the section in 1918. He served as a member of the Council on Scientific Assembly from its beginning in 1915 until 1927. His sound advice was often sought in discussions concerning this assembly, which is an outstanding example of the value of demonstrations in the dissemination of the knowledge of newer things in medicine and the necessity of postgraduate teaching. He served as President of the American Medical Association during the year of 1931-1932. In this capacity he served with high distinction, ever mindful of the needs of the members of this organization and the objectives which they should hope to attain if they were to render the highest type of medical service.

Constant demands were made on him to appear before medical societies. Facts were presented so clearly by him, in such a simple but striking way, that he became a postgraduate teacher of great renown. He stood on solid ground surgically and was never greatly moved by surgical fads. Having the gift of critical ability, he dealt with fundamentals. Listeners knew that he spoke with the authority of experience and strove to sit at his feet.

He was a member of the American Surgical Association, the American College of Surgeons, the Minnesota Academy of Medicine, the Minnesota Pathological Society, the Western Southern and Interurban surgical associations, the American Society of Clinical Surgery and the

carbon dioxide with air, and he concluded "The calculation of the relative amounts of air and  $\text{CO}_2$  necessary to maintain proper pressure relations after withdrawing the spinal fluid was so difficult as to make the method impossible. The reactions were severe and served to emphasize the necessity of using insoluble gases to replace the spinal fluid." He next used nitrogen, and in about 40 patients he obtained more promising results. He noted that in most cases headache was less severe than it was following the use of air but stated "The difference between nitrogen and air, however, cannot truthfully be said to be very striking." Finally, helium was used in 12 cases. With the use of this gas the author reported that headache was "almost uniformly less severe than with the other gases" and that the results were "encouraging." He stated "In conclusion nothing substantial has been found to obviate the discomforting post-injection headache. The displacement of the cerebrospinal fluid by gases other than air holds a little promise for less severe reactions, but headaches of moderate severity are still present in almost every case."

In this review the work of Laruelle<sup>30</sup> might also be mentioned, in 1931 Laruelle reported the use of small amounts (from 5 to 15 cc) of air, with the idea of avoiding the ill effects and dangers of the usual injection of air. He believed that such small injections were usually adequate from a diagnostic standpoint. However, most authors have agreed with Grant,<sup>31</sup> who stated "But by far the larger number of the mistakes and failures accurately to localize the lesion have been due to incomplete filling of the ventricular system with air."

#### THEORETICAL CONSIDERATIONS

The ideal method of demonstrating the ventricular system would be one which would require no more trouble than that involved in making roentgenograms of the skull. Such a possibility has indeed been suggested by Dr. Naffziger,<sup>32</sup> who pointed out that the peculiar properties of neutrons, in being blocked by water and yet penetrating more dense substances, might conceivably be used for this purpose. However, further investigation<sup>33</sup> revealed that the blocking effect is an atomic mechanism, the light atoms such as hydrogen and oxygen being more effective than those of calcium, etc. When it is remembered that the tissue of the brain is about 84 per cent water and that the remainder is composed chiefly of lipoids, made up almost entirely of the light

30 Laruelle, L. Le repérage des ventricules cérébraux par un procédé de routine, *Presse méd* **39** 1888 (Dec 23) 1931

31 Grant, F. C. Encephalographie et ventriculographie, *Rev. neurol* **2** 370 (Oct) 1931

32 Naffziger, H. C. Personal communication to the author

33 Lawrence, Ernest. Personal communication to the author

## EXPERIMENTAL ENCEPHALOGRAPHY WITH ANESTHETIC GASES

ROBERT B AIRD, M D

SAN FRANCISCO

Following the introduction of ventriculography in 1918 and encephalography in 1919 by Dandy, these procedures received wide attention and trial. Early mistakes were soon corrected, and the tests have become relatively safe procedures to which the neurosurgeon does not hesitate to subject his patient if he believes them to be indicated.

However, the injection of air into the ventricular and subarachnoid spaces carries with it certain unpleasant effects which appear to be inevitable.

The injection of air almost invariably causes an acute reaction, characterized by severe headache and occasionally nausea, vertigo, vomiting, profuse perspiration and more or less shock. Anesthesia alone is capable of overcoming this, and when an injection of air is made in a patient whose condition is already unfavorable, the procedure becomes of major importance. The acute reaction generally lasts from six to eight hours.<sup>1</sup> More serious reactions are avoided by the proper selection of patients and an improved technic of injection.

Another unfortunate feature of the injection of air is its prolonged presence. It is thought that air is absorbed from the human subarachnoid spaces in from twelve to twenty-four hours.<sup>2</sup> Air disappears from the ventricles much more slowly. Reports of its presence for from seven to ten days and even longer may be found in the literature. Headache and other symptoms, less severe than in the initial acute reaction, are usually prolonged one or two days.<sup>3</sup> The fact that

From the Department of Surgery of the University of California Medical School.

This work has been conducted under grants from the Christine Breon Fund for Medical Research and the Dudley Cates Donation for Neurologic Research of the University of California Medical School.

<sup>1</sup> Pendergrass, E P. The Value of and Indications for Encephalography and Ventriculography, with Discussion of the Technic, *S Clin North America* 10 1461, 1930.

<sup>2</sup> Friedman, E D. Further Experiences with Encephalography. Evaluation in Clinical Neurology, *Internat Clin* 1 54 (March) 1930. Weigeldt, W. Die Bedeutung der Luftemblasung für Hirn- und Rückenmarksdiagnostik, *Deutsche Ztschr f Nerven* 77 165, 1923.

<sup>3</sup> Pancorist, H K, and Fay, T. Encephalography. Roentgenological and Clinical Considerations for Its Use, *Am J Roentgenol* 21 421 (May) 1929. Pendergrass.



From theoretical considerations it would seem possible that a gas more suitable than air might be found for encephaloventriculography. The ideal, of course, would be a gas which would give roentgen results comparable to those gained with air and yet involve no more distress, shock or outlay of time and expense than would be incident to the necessary mechanical methods of effecting the injection, namely, lumbar puncture or incision of the scalp and making holes in the skull with a bur with the use of local anesthesia. A gas approaching this ideal should be nonirritative, entirely safe and easy to handle, it should fill and outline the ventricular and subarachnoid spaces and give a good contrast shadow for roentgen study, it should cause little or no immediate reaction and a minimum degree of shock, and it should be absorbed within a few hours, so that increased pressure and other possible ill effects of its prolonged presence might be avoided.

If, in addition to these points, the agent were of such a nature that it would have a sedative or narcotic effect, it would approach even closer to the theoretical ideal, since such an effect might conceivably overcome much of the pain and distress incident to the procedure.

It occurred to me that an anesthetic gas might qualify as the desired agent. Since only a limited amount of gas can be injected and since this is relatively inert except as absorbed, it seemed conceivable that even strong anesthetic gases might prove safe, any sedative or narcotic effect being the result of its absorption and concentration in the central nervous system. Also, the local effect of such a gas on the nerve tissues with which it was in direct contact might be to deaden them and abolish noxious reflexes, in contrast to the effect of ordinary gases. The handling of the gas and the roentgen results would be comparable with those achieved by the use of air. The duration of its presence would depend on such factors as its rate of diffusion and solubility in the spinal fluid and in the lipoids. The investigation of such a possibility seemed worth while.

#### METHOD

The method developed for this investigation, as well as some of the preliminary results, have already been reported briefly.<sup>37</sup> Encephalography, because of its comparative simplicity, was favored over ventriculography as the method of choice for this investigation.

Preliminary tests were carried out on cats. Their bony skulls and small ventricles proved a great handicap from the standpoint of obtaining satisfactory roentgenograms. Dogs were much more satisfactory and the work to be reported was based entirely on their use as laboratory animals.

After early trials, suboccipital puncture was discarded in favor of lumbar puncture, the latter proving safer and allowing more free manipulation of the head,

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37 Aird, R. B. Experimental Encephalography with Anesthetic Gases, *Proc Soc Exper Biol & Med* **31** 715, 1934.

Iodized poppy-seed oil 40 per cent was used for spinal epidural and subarachnoid injection as early as 1923 by Seard and Forestier<sup>7</sup> and later was used intraerally in various ways by Schuster,<sup>8</sup> Rimbaud, Lamarque and Jambon,<sup>9</sup> Schaeffer and Baron,<sup>10</sup> Gortan and Saiz,<sup>11</sup> Sicard and Forestier,<sup>12</sup> Mayer,<sup>13</sup> Haguénau and Gall,<sup>14</sup> Balado,<sup>15</sup> Morea,<sup>16</sup> Obarrio and Orlando<sup>17</sup> Carrillo<sup>18</sup> and Castex and Romano<sup>19</sup> The results have been rather unsatisfactory from a roentgenologic standpoint Reactions, usually headache and fever, were reported by all except the South American authors In 1931 Bruskin and Propper<sup>20</sup> carefully studied the pathologic effects of iodized poppy-seed oil 40 per cent over prolonged periods in dogs Granulomatous and absorptive reactions were observed in the meninges Vascular reactions and changes in the cortical cells were noted also These authors expressed the opinion that such manifestations in the meninges and brain were typical of a foreign body reaction

7 Sicard, J A, and Forestier, J L'huile iodée en clinique Applications thérapeutiques et diagnostiques, Bull et mem Soc med d hop de Paris **47** 309 (Feb 23) 1923

8 Schuster, J Ventriculographie mit Lipiodol ascendenst und descendenst, Klin Wchnschr **4** 2064 (Oct 22) 1925

9 Rimbaud, Lamarque and Jambon Lipiodol ascendant intra-ventriculaire Presentation de clichés, J de radiol et d'electrol **9** 450 (Oct) 1925

10 Schaeffer, H, and Baron, P Le lipiodol ascendant dans la localisation des tumeurs cerebrales Son interet et ses dangers, Medecine **7** 391 (Feb) 1926

11 Gortan, M, and Saiz, G Encefalografia e lipiodol ascendente, Policlinico (sez med) **33** 312 (June) 1926

12 Sicard, J A and Forestier, J Roentgenologic Exploration of Central Nervous System with Iodized Oil (Lipiodol), Arch Neurol & Psychiat **16** 420 (Oct) 1926

13 Mayer, E G Zur Verwendung des aufsteigenden Jodols für die Röntgen-diagnostik, Fortschr a d Geb d Röntgenstrahlen **38** 619 (Oct) 1928

14 Haguénau, J, and Gall Exploration lipiodolée rachimedullaire et cranio-cerebrale, J de radiol et d'electrol **13** 369 (July) 1929

15 Balado, M Radiografia del tercer ventriculo, mediante la inyeccion intra-ventricular de lipiodol, Arch argent de neurol **2** 69 (March) 1928, Anatomia clinica y radiologica del tercer ventriculo, Semana med **1** 413 (Feb 12) 1931

16 Morea, R Técnica y resultados de la ventriculografia, Semana med **1** 281 (Jan 28) 1932

17 Obarrio, J M, and Orlando, R La visualizacion del 3° y 4° ventriculos con lipiodol, Prensa med argent **16** 1401 (March 30) 1930

18 Carrillo, R La radiografia del cuarto ventriculo, Semana med **2** 719 (Sept 3) 1931

19 Castex, M R, and Romano, N Un caso insolito de bala en el cerebro, utilidad de la ventriculografia con aceite iodado en la interpretacion diagnostico-topografica, Prensa med argent **17** 333 (July 30) 1930

20 Bruskin, J, and Propper, N Experimentelle Myelo-Encephalographie an Hunden und über den Einfluss von Jopidin und Lipojodol auf das Rückenmark, Gehirn und dessen Haute, Ztschr f d ges exper Med **75** 34, 1931

the injecting syringe and connected by tubing to the controlling valve<sup>40</sup> of the gas tank afforded a simple and convenient closed system for handling the gases. Replacement of the spinal fluid by gas was carried as far as possible, usually until bubbles returned through the needle. Then the needle was withdrawn, and another lateral roentgen view of the skull was made. If the ventricular outline appeared, other views were taken to follow the course of the injection. Throughout the entire procedure, pulse, respiration, color, reflexes and muscle tension were observed closely and recorded.

With improvements in technic, standardization of routine and experience, this method proved satisfactory for determining the following information on the various anesthetic gases: (1) ease of handling, (2) early irritative effect, (3) sedative or narcotic effect, (4) after-effects, both immediate and late, (5) safety, and (6) roentgen results, including the time of absorption.

### OBSERVATIONS

Repeated encephalograms were obtained in this manner on the same animal to compare under as nearly identical conditions as possible the effects of the various gases. The results obtained will be discussed briefly. The observations are summarized in table 1.

An injection of air was initially performed in all animals as a standard by which the results obtained with the other gases could be compared. Aside from a few early, uncontrolled injections, thirty-eight controlled injections of air have been made in twenty-four dogs. In two of the dogs air was not seen in the roentgenogram on two different trials, as well as in subsequent injections of gas, and therefore the animals were discarded. In three others air was not evident in one of two trials, and in a fourth there was questionable roentgen evidence of air in one of three trials. Seventeen of the animals were aroused as soon as the injection of air was started, and, except in four or five instances in which there was no apparent effect and in one instance in which the effect could not be judged, all were more widely awake at the end of the injection and were easily aroused by manipulation of the needle or by injection under pressure. Prolonged depression, characterized by obvious hypo-activity and distress on movement, was observed in all the thirty dogs showing successful filling. The head was usually held stiffly in one position (fig 1), and movement of the animal aroused an objecting whine. This reaction persisted ordinarily from one to three days. In seventeen animals followed by roentgen examination to determine how long the air remained, the average was slightly under a week, with extremes of from one to two days and from thirteen to fourteen days, depending on the initial degree of filling. The similarity of the experimental results to those found in encephalography in man seemed close in all respects.

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<sup>40</sup> This was lent by the Certified Products, Inc., San Francisco.

Jungling<sup>26</sup> in 1922 reported the use of oxygen in pneumography. His report, however, was chiefly concerned with the technique of injection, and the use of oxygen as compared with the use of air was mentioned only briefly. He noted no bad results, e. g., headache, vomiting or increase of symptoms, with the use of oxygen and expressed the opinion that sterile oxygen is preferable, because its use insures against infection and the gas is more quickly absorbed than air.

Denk<sup>27</sup> in 1923 also used oxygen. This author reported severe reactions following encephalography and relatively slight reactions following ventriculography, which method he therefore greatly favored. His use of oxygen was incidental, apparently, and was prompted more by the fear of air embolism in ventriculography than by any merit that oxygen as a gas might have over air. A controlled study of oxygen as an agent for encephaloventriculography was entirely lacking. No adequate comparison was made with the effect of air, reactions to it or the length of time it was present.

Oxygen is being used experimentally in the neurosurgical clinic of Penfield and Cone in Montreal, with favorable results. Lessened reactions have been reported,<sup>28</sup> with a corresponding decrease in the necessary period of hospitalization from about four or five days to three days.

In April 1933 Liberson<sup>29</sup> reported the use of air, carbon dioxide, nitrogen and helium in encephalography in man. He used a modification of the Bingel method, the transfer of gas and of spinal fluid in this closed system being effected by means of a double (a needle within a needle) lumbar puncture needle. Liberson expressed the opinion that this simultaneous replacement saved the patient considerable shock and discomfort. Previous to injection, the gas was passed through water baths to free it from all possible dust. The author expressed the belief that this somewhat lessened the reaction after the injection. By the use of this method the injection of air in no case caused shock requiring treatment, and there were no fatalities in 210 cases. Headache, however, was almost always present, being constant and severe for from five to six hours and persisting in less severe form for from one to four days. Carbon dioxide was used in 3 cases. Because of its great solubility in spinal fluid Liberson was forced to mix the

26 Jungling, O. Zur Technik der Sauerstoff-füllung der Hirnventrikel zum Zwecke der Röntgendiagnostik, *Zentralbl. f. Chir.* **49** 833 (June 10) 1922.

27 Denk, W. Ueber Encephalographie und ihre Ergebnisse, *Ztschr. f. ärztl. Fortbild.* **20** 426, 1923.

28 Jones, O. W. Personal communication to the author.

29 Liberson, F. Use of Various Gases in Encephalography. Summary of Two Hundred and Ten Cases, Using Simultaneous Displacement Apparatus, *Am. J. M. Sc.* **185** 478 (April) 1933.

Because the use of oxygen has been reported on favorably,<sup>26</sup> is at present being used in at least one well known neurosurgical clinic and probably represents about as great an improvement over air as can be obtained with an ordinary gas, a few trials were made on dogs for the sake of comparison. Four injections were made in four different animals. Rather marked irritation resulted in two, no apparent effect was observed in a third, and the fourth was too deeply under an initial narcosis for one to tell what the effect was. Good roentgen results were obtained, the gas remaining for approximately one day. In one dog a suggestive depression, such as follows the use of air, persisted for nearly two days.

Ether, di-vinyl oxide<sup>41</sup> and ethyl chloride may be dismissed as being too dangerous for the purposes of encephalography. Di-vinyl oxide and ether required special heating coils to volatilize<sup>42</sup> them to body temperature before injection. Ethyl chloride alone remained



Fig 1—Postinjection depression exhibited thirty hours after air was injected

unabsorbed sufficiently long to make it practical from the standpoint of roentgenography. The immediate irritative effect of these gases was marked, and their injection was followed by rapid and deep anesthesia tending to induce respiratory paresis. Paresis of the hindleg, which required several days to clear, followed the injection of di-vinyl oxide and ether gas in an unusually high percentage of the animals.

Vinyl chloride,<sup>43</sup> used five times in four dogs, elicited a marked irritative reaction throughout the period of injection in all instances. The pulse and respiratory rates were strikingly affected, being raised to

41 Leake, C D, Knoefel, P K, and Guedel, A E. Anesthetic Action of Divinyl Oxide in Animals, *J Pharmacol & Exper Therap* **47** 5 (Jan) 1933. The preparation was obtained through the courtesy of Dr. Randolph T. Major, director of the laboratory of pure research, Merck & Company.

42 The boiling points are given in table 5.

43 Patty, F A, Yant, W P, and Waite, C P. Acute Response of Guinea Pigs to Vapors of Some New Commercial Organic Compounds, *Pub Health Rep* **45** 1963 (Aug 22) 1930. The gas was obtained through the courtesy of Dr. C D Leake, Department of Pharmacology, University of California Medical School.

atoms, hydrogen, carbon and oxygen, the contrast conceivably obtainable by this method e g., between the ventricles filled with cerebrospinal fluid and the surrounding brain, probably would be inadequate Other considerations such as the present insufficient production of neutrons and their unknown biologic destructiveness and photo-activity prevent the experimental trial of this idea, at least for the present

Another method only slightly less ideal would be the discovery of a radiopaque agent which on intravenous injection would be concentrated in the ventricular spaces, such as tetra-iodophenolphthalein in cholecystography or iso-iodoikon in urography Since, as suggested by Mestrezat<sup>34</sup> and more recently emphasized by Fremont-Smith and his various co-workers,<sup>35</sup> cerebrospinal fluid is a dialysate in osmotic equilibrium with the blood plasma and is analogous to the intercellular fluids rather than a true secretion such as bile,<sup>36</sup> a concentration of any agent in the ventricles seems unlikely On the contrary, widespread distribution in intercellular fluids, as well as elimination by the kidneys, etc., would probably operate to dissipate effectively such an injection of dye Such an intercellular distribution of the cerebral tissues of loose texture would further tend to obscure any contrast between the ventricles and the surrounding brain Finally, the possibility of a concentration of a radiopaque dye in the cerebrospinal and intercellular fluids which would be sufficient to give an adequate contrast shadow between them and yet be nontoxic seems highly unlikely

The injection of radiopaque fluids into the ventricles has been considered already, and the limitations of this method need not be stressed further

Attention, then, may be limited to the more practical method of replacing the cerebrospinal fluid by gases

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34 Mestrezat, W. Le liquide cephalo rachidien, milieu interieur de l'organisme, *Rev. neurol.* **1** 64 (Jan.) 1927

35 Fremont-Smith, F. Nature of Cerebrospinal Fluid, *Arch. Neurol. & Psychiat.* **17** 317 (March 1927) Fremont-Smith, F., and Forbes, H. S. Intra-Ocular and Intracranial Pressure. Experimental Study, *ibid.* **18** 550 (Oct.) 1927 Fremont-Smith, F., and Karbie, L. S. The Intracranial Pressure in Health and Disease, Baltimore, Williams & Wilkins Company, 1927, chap. 7 Fremont-Smith, F., and Dailey, M. E. The Effect of Protein Concentration upon the Chloride Equilibrium Between Plasma and Cerebrospinal Fluid, *J. Pharmacol. & Exper. Therap.* **27** 255, 1926

36 The concentration of such agents as iso-iodoikon in glomerular filtrate, which bears some analogy to cerebrospinal fluid and intercellular fluid,<sup>35</sup> would not be possible in the cerebral ventricles, since the concentration in the kidneys is effected by the tubular absorption of the salts essential for the maintenance of the body economy along with sufficient water to keep these salts in isotonic solution The unabsorbed waste products and dye thus left in concentrated form escape to the renal pelvis as urine

Ethylene<sup>46</sup> and nitrous oxide may be considered together, since the results obtained with them were similar. The quick, easy induction, the nontoxicity, the excellence of anesthesia and the rapidity of recovery obtained with them as general anesthetics recommend both for trial. Ethylene was used twenty-six times in twelve different dogs, and nitrous oxide, twenty-two times in eleven dogs. Irritation, possibly attributable to the injection of these gases, was noted in a few instances, but it was slight and usually was followed by a sedative effect. The narcotic effect of ethylene seemed a little more intense than that of nitrous oxide. In all forty-eight injections no alarming symptoms were observed, even though the injections were carried as far as possible in all cases. The roentgen results were satisfactory, with nitrous oxide remaining present approximately one hour, and ethylene, two hours. Because of the nonirritative action, the safe sedative effect, the lack of after-effects and the good roentgen results obtained with these gases, additional studies were carried out.

#### FURTHER SPECIAL STUDIES

*Cytologic and Pressure Reactions of Cerebrospinal Fluid to Air, Nitrous Oxide and Ethylene*—Following preliminary and incomplete studies of the cell reactions of cerebrospinal fluid to the injection of air, ethylene and nitrous oxide, a carefully planned series of injections in three animals was carried out, with a follow-up observation of the cell count and pressure reactions.

In one series (dog 42) encephalography by the lumbar route was carried out with a sedative dose of morphine. In a second series (dog 66) encephalography was carried out by the lumbar route after a sedative dose of sodium amytal. In the third animal (dog 45) injection by the cisternal route was carried out, with the animal under sodium amytal anesthesia. Also, for the sake of comparison, an injection of nitrous oxide was made in this animal by the lumbar route after a morphine sedative was given (table 3). Determinations of the cell count and pressure of the cerebrospinal fluid were made before the injections and were repeated (by simple lumbar puncture, with the same sedative or anesthetic, respectively) on the first, third and seventh day following the injections.

With these same routes, an initial control series of tests was made on each animal, the cell and pressure reactions being followed without an injection of gas. Moderate cell counts were obtained in the two animals on which puncture had been done by the lumbar route one or

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<sup>46</sup> Gwathmey, I. T. *Anaesthesia*, ed 2, New York, The Macmillan Company, 1924, p 711. The preparation was obtained through the courtesy of the French Oxygen Co., San Francisco.

done to aid the drainage of cerebrospinal fluid. However, a few tests carried out by cisternal puncture for later special studies will be reported.

Because repeated punctures on the same animal were desirable from an economic standpoint as well as for the sake of comparing more adequately the effects of the various gases, simple lumbar laminectomy was performed on each of the dogs to facilitate the punctures. Punctures were not attempted until the laminectomy wounds were well healed, usually not before three weeks following the operation.

To secure the animal in a comfortable position which was satisfactory for lumbar puncture and also to give maximum access for manipulation and the observation of reactions, a special table of simple construction was devised. It consisted of a floor hinged to a base, so that the animal, strapped on its side to the floor, could be tilted to any desired angle up to 45 degrees. Two side boards nailed to the floor gave support to the back and buttocks. A cut in the backboard allowed ample exposure about the lumbar area for punctures. With this table, the operator on one side could perform the lumbar puncture and injection of gas, while on the other side the attendant could watch the animal, rotate the head and chronologically record events. Theoretically, such a reclining posture is not as good as the vertical or sitting position for encephalography. However, it has been used with success in some clinics,<sup>38</sup> and in this work it proved satisfactory.

At first, enough morphine was administered to deaden ordinary pain and keep the animal quiet but not sufficient to conceal the possible irritative or sedative effects of the injected gases. It was noted, however, that the deep state of anesthesia induced by some of the injected gases tended to paralyze the respiratory center. It thus became necessary to select a sedative which would not have the depressing effect of morphine on respiration. Phenobarbital was tried, but it proved rather unsatisfactory. A state of light anesthesia induced by sodium amytal finally proved satisfactory, and the major portion of the work was done with this sedative. The dose necessary varied with the animal, but amounts varying from 22 to 32 mg per kilogram of body weight were found satisfactory. With such doses the animal was quiet, good roentgenograms could be obtained easily, the injection of procaine hydrochloride and puncture of the meninges aroused the animal only briefly and yet reflexes, muscle tension and often a fair degree of consciousness remained, so that superimposed irritative or narcotic effects of the injected gases usually could be readily determined.

A 10 milliamperere dental roentgen ray machine<sup>39</sup> with an automatic time control gave satisfactory roentgenographic results. The automatic timer, kept constant for each dog, the use of one cassette for the films and general standardization of the technic contributed to give a good series of comparable roentgenograms. Single lateral views proved most satisfactory for visualization of the gas-filled ventricles and seemed adequate for the comparative results essential in the study.

The usual routine of encephalography was as follows. After the intravenous administration of sodium amytal and the making of an initial plate of the skull as a control, the dog was strapped on its side to the table described previously, and with aseptic technic and with local anesthesia a lumbar puncture was performed. The table was elevated, and intermittently between collections of spinal fluid the gas to be tested was injected slowly, by means of a syringe, into the subarachnoid spaces. Rotation of the head aided drainage. A three-way pet-cock attached to

38 Branch, C. D., Cutler, E. C., and Zollinger, R. Experiences with Encephalography, *New England J. Med.* 207:963 (Dec. 1) 1932.

39 This was lent by the Department of Dental Research, Hooper Foundation, University of California Medical School.



TABLE 2.—Comparative Study of Cell Count and Pressure of the Cerebrospinal Fluid and Roentgen Observations on Subarachnoid and Ventricular Irrilling After Encephalography with Au, Nitrous Oxide and Ethylene

	Control						Air						Nitrous Oxide						Ethylene					
	Date	Total Cell Count	Poly morpho nuclears	Lymphocytes	Monocytes	Pressure	Date	Total Cell Count	Poly morpho nuclears	Lymphocytes	Monocytes	Pressure	Date	Total Cell Count	Poly morpho nuclears	Lymphocytes	Monocytes	Pressure	Date	Total Cell Count	Poly morpho nuclears	Lymphocytes	Monocytes	Pressure
Dog 42 Lumbar puncture with morphine sedative Cerebrospinal fluid	3/14	1	0	0	100	135 to 155	4/4	7	9	55	96	118	4/28	5	30	0	50	110						
	3/15	29	10	30	10	175	4/5	1120	81	11	8	110	3/22	182	71	23	6	195						
	(? bloods)	81	70	10	20	100	4/7	55	63	21	16	82	4/21	193	61	14	22	200 to 210						
	3/17	0	0	0	0	140	4/11	115	66	1	30	105	4/28	5	70	0	70	110						
	3/21	0	0	0	0	140	4/14	2	9	9	?	?	110											
Roentgen findings	No gas injected																							
Cerebrospinal fluid							5/16	16	17	66	17	132	5/16	2	0	0	100	195						
							5/17	1,271	85	12	115	162	5/17	0	0	0	100	195						
							5/19	701	75	6	19	170	5/19	1,177	80	12	8	130						
							5/23	28	0	88	12	105	5/23	265	65	22	13	170						
								5/26	5	20	80	0	125	5/26	17	13	51	6	137					
Roentgen findings	Subarachnoid air and massive ventricular filling																							
Dog 45 Gisternal puncture with methyl anesthesia Cerebrospinal fluid	4/25	2	0	0	100	165	5/9	5	6	0	100	80	5/2	3	0	0	50	85						
	4/26	1	0	0	100	70	5/10	910	81	14	17	85	5/10	201	9	40	50	85						
	4/28	6	0	0	100	95	5/12	381	51	46	11	88	5/12	8	0	100	0	85						
							5/16	11	27	53	20	67	5/16	5	0	100	0	80						
								5/23	12	0	100	0	80	5/23	9	20	11	57	85					
Roentgen findings	Subarachnoid gas and massive ventricular filling																							
Dog 66 Lumbar puncture with amylal sedative Cerebrospinal fluid	3/21	0				140	5/2	15	0	100	0	63	3/23	3	50	0	50	115						
	3/22	85	72	14	14	195	5/3	282	65	15	20	46	3/29	176	88	6	6	80						
	4/24	25	50	22	15	110	5/5	126	26	53	21	11	5/31	100	50	32	18	78						
	4/28					115	5/9	78	20	60	20	68	5/11	11	20	40	40	75						
								5/12	130	17	51	32	80	5/12	18	13	71	13	69					
Roentgen findings	Subarachnoid gas and slight ventricular filling																							
Dog 66 Lumbar puncture with amylal sedative Cerebrospinal fluid	3/21	0				140	5/2	15	0	100	0	63	3/23	3	50	0	50	115						
	3/22	85	72	14	14	195	5/3	282	65	15	20	46	3/29	176	88	6	6	80						
	4/24	25	50	22	15	110	5/5	126	26	53	21	11	5/31	100	50	32	18	78						
	4/28					115	5/9	78	20	60	20	68	5/11	11	20	40	40	75						
								5/16	98	26	41	31	87	5/16	18	13	71	13	69					
Roentgen findings	Subarachnoid gas and (?) slight ventricular filling																							
Dog 66 Lumbar puncture with amylal sedative Cerebrospinal fluid	3/21	0				140	5/2	15	0	100	0	63	3/23	3	50	0	50	115						
	3/22	85	72	14	14	195	5/3	282	65	15	20	46	3/29	176	88	6	6	80						
	4/24	25	50	22	15	110	5/5	126	26	53	21	11	5/31	100	50	32	18	78						
	4/28					115	5/9	78	20	60	20	68	5/11	11	20	40	40	75						
								5/16	98	26	41	31	87	5/16	18	13	71	13	69					
Roentgen findings	Subarachnoid gas and (?) slight ventricular filling																							

TABLE 1—Comparative Observations on the Results of Experimental Encephalography

Gas	Number of Injections <sup>4</sup>	Handling	Safety	Roentgen Results		Effect on Animal			
				Ventricular Filling	Average Time Gas Was Present	Immediate Irritation	Sedative or Anesthetic	Prolonged Depression	Other Effects
Air	38	Easy	Safe	Good	7 days	72	0	100% of successful injections <sup>5</sup> (1 to 3 days)	Spinal fluid cell count, 1,200
Acetylene	6	Easy	Safe	? Satisfactory	20 to 30 min	2	2 (?) sedative 2 sedative 2 anesthetic	0	
Cyclopropane	4	Easy	Safe	Good	1 day	2	Slight, if any	0	Spinal fluid cell count, 1,600
Di vinyl oxide	7	Difficult	Very dangerous	Satisfactory	15 to 18 min	6	7 anesthetic	0	Paresis of hindleg in 3 cases (death (respiratory paresis) in 2 cases)
Ether	7	Difficult	Dangerous	0	?	7	2 sedative 4 anesthetic	0	Paresis of hindleg in 3 cases death (respiratory paresis) in 1 case
Ethyl chloride	10	Fairly easy	Very dangerous	Good	15 to 45 min	10	10 anesthetic	0	Death (respiratory paresis) in 1 case
Ethylene	26	Easy	Safe	Good	2 hours	2 (?) ? slight	2 (?) sedative 20 sedative 2 (?) anesthetic	0	Spinal fluid cell count, 1,700 to 2,000 (?)
Nitrous oxide	22	Easy	Safe	Good	1 hour	2 (?) ? slight	1 (?) sedative 1, sedative	0	Spinal fluid cell count 1,100
Oxygen	4	Easy	Safe	Good	1 day	2	0	1 (1 to 2 days)	Spinal fluid cell count, 1,700
Vinyl chloride	5	Easy	Slightly dangerous	Satisfactory	20 min	,	1 anesthetic	0	Pulse and respiratory rates markedly raised



Fig 4 (dog 42) —Massive ventricular filling with nitrous oxide



Fig 5 (dog 42) —Massive ventricular filling with ethylene

unusually high levels. In one animal the pulse rate rose to 190 and the respiration became greatly depressed and at one time almost stopped. Cyanosis appeared. There was a complete loss of muscular tone and reflexes. Recovery occurred in twenty minutes. Apparently this gas must also be classed as dangerous. The foregoing reaction, in addition to its marked irritative effect and brief presence in the ventricles (table 1), precludes its use in encephalography.

The nontoxicity, low solubility and rapid and excellent narcosis of acetylene<sup>44</sup> suggested that it might prove a desirable gas for encephalography. A tank of commercial acetylene, like that used for welding, was rented, and without purification the gas was injected six times in four dogs. In spite of the fact that the unpurified gas was used, no irritative reaction was observed in any of the animals. The reaction to the injection was not remarkable. The pulse rate usually rose a little, and respiration, except in one dog, either was not affected or was decreased. The animals became more quiet and relaxed, and fairly definite anesthesia, which lasted about twenty minutes, was obtained in three animals. In one of the other three dogs, a sedative effect was definitely obtained, while in two, such an effect was questionable. The roentgen results, however, were disappointing. The gas disappeared in less than half an hour, and its value for the purpose of encephalography therefore seems questionable.

Cyclopropane<sup>45</sup> was injected four times in three animals, with successful filling of the ventricles in each instance. The gas remained present about one day. A questionable sedative effect was obtained in one animal. Irritation on injection was observed in two of the dogs (tables 1 and 4). Although this gas is apparently a great improvement over air and is probably superior to oxygen, it seems definitely inferior to either ethylene or nitrous oxide, the observations on which will be discussed in the next paragraphs.

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44 Gauss, C. F., and Wieland, H. Ein neues Betaubungsverfahren, *Klin Wchnschr* **2** 113 (Jan 15), 158 (Jan 23) 1923. Wieland, H. Acetylene Anaesthesia, *Brit J Anæsth* **2** 142 (Jan) 1925. Mallebrein, O., and Maier, J. H. Zweitausend eigene Narzylenbetaubungen, *Deutsche med Wchnschr* **51** 1521 (Sept 11), 1567 (Sept 18) 1925. Goldman, J. D. Conclusions from Extended Experiments with Nitrous Oxide, Acetylene, Ethylene, Oxygen Anaesthesias, *Anæsth & Analg* **7** 219 (July-Aug) 1928.

45 (a) Henderson, V. E., and Lucas, G. H. W. Cyclopropane. New Anaesthetic, *Anæsth & Analg* **9** 1 (Jan-Feb) 1930. (b) Henderson, V. E., and Johnston, J. F. A. Anesthetic Potency in the Cyclo-Hydrocarbon Series, *J Pharm & Exper Therap* **42** 257 (July) 1931. The preparation was obtained through the courtesy of the Shell Development Company, Emeryville, Calif. The gas is manufactured by the Ohio Chemical Company, Cleveland.

four which had injections of oxygen (table 4). Although the results perhaps have not the same comparative significance as those of the carefully planned tests just described, it is of interest to note that the two good injections of cyclopropane caused peak cell counts of 1,511 and 1,613, respectively, and that one of these counts was carried out on one of the same animals and under conditions comparable to those maintained in the well controlled series. The uniformly high counts obtained following the injection of oxygen are also noteworthy.

The comparative peak cell counts shown in table 1 represent the reaction to maximal and roughly equal injections of gas as checked by roentgenogram but, for the reasons already given, must be regarded only as suggestive.

No striking results were obtained in the observations on pressure. The changes were inconstant, and pressures lower as well as higher than the presumed normal were found after the injection of various

TABLE 3—*Observations on Dog 45 After Lumbar Encephalography with Nitrous Oxide by Puncture with a Morphine Sedative*

	Data	Total Cells	Differential Cell Count, Percentage			Pressure
			Poly morpho nuclears	Lymphocytes	Mono cytes	
Data on cerebrospinal fluid	3/28	5	40		60	175
	3/29	1,086	71	13.5	15.5	160
	3/31	135	40	20	40	150
	4/4	64	10	15	75	135
Röntgen findings	Subarachnoid gas and slight ventricular filling					

gases. Although the majority of tests suggest a rise of spinal fluid pressure following the injection of gas, no satisfactory correlation can be made either with respect to the time of injection or with respect to the type of gas injected. Such uncontrolled variants as the degree of narcosis and the disturbance caused by puncture seem the most likely explanations of the inconstant results obtained.

Differential cell counts revealed an early polymorphonuclear leukocyte reaction, which persisted usually past the third day after the injection. Mononuclear cells were usually in predominance by the seventh day. The type of gas used apparently caused no characteristic differential cell reaction.

*Pathologic Studies*—Pathologic studies<sup>48</sup> on the brain, cord and meninges were carried out on nine dogs following the repeated injections of air, nitrous oxide and ethylene. Three animals were used for each

48 Prof. C. Connor and members of the department of pathology assisted in the preparation of the routine hematoxylin and eosin and prussian blue stains, and Dr. O. W. Jones, of the department of surgery, and Dr. I. F. Rinehart, of the department of pathology, gave advice and help.

two days previously. The cell count was normal in both animals within four days. The cell counts were within normal limits in the animal on which puncture had been carried out by the cisternal route, regardless of the time of the preceding puncture (table 2).

The order of the injections of the gases was varied in the different animals. A complete second series of tests was made on one animal, which proved most suitable for the study (dog 42, lumbar route with morphine sedative), the order of injections of gas being varied in the repeat series.

The results of these studies are shown in table 2.

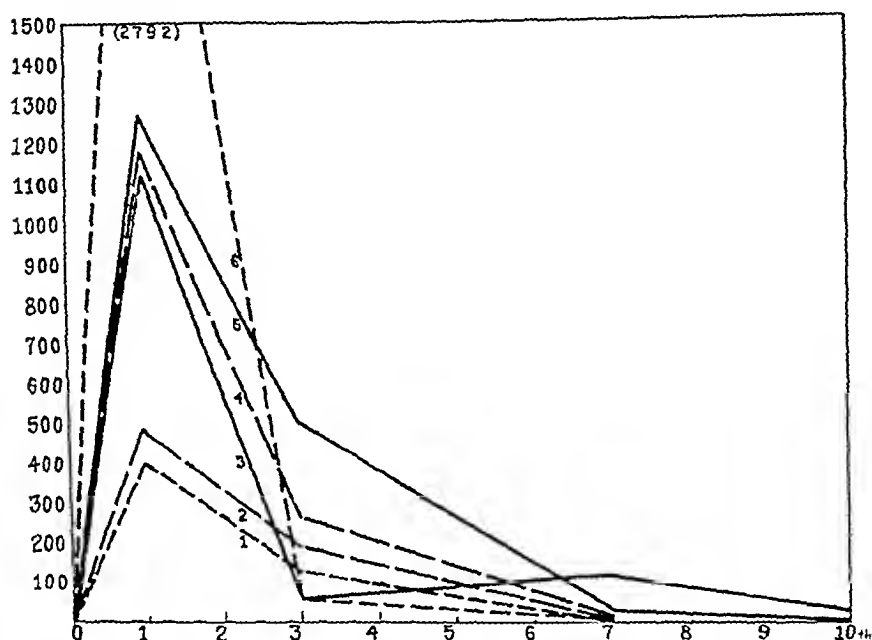


Fig 2—Total cell count of the cerebrospinal fluid after encephalography with air, nitrous oxide and ethylene in dog 42. Injection was made by lumbar puncture with a morphine sedative. The ordinate indicates the total cell count and the abscissa the days after injection. Observations were as follows:

Injection	Date	Gas	Roentgen Findings
1	4/25	Ethylene	Subarachnoid (cisterna magna) filling
2	3/21	Nitrous oxide	Slight ventricular filling (fig 3)
3*	4/ 4	Air	Good ventricular filling
4	5/ 2	Nitrous oxide	Massive ventricular filling (fig 4)
5	5/16	Air	Massive ventricular filling (fig 6)
6	3/28	Ethylene	Massive ventricular filling (fig 5)

\* The tap on the third day following injection 3 was slightly bloody. The value assigned is therefore questionable.

The solid line indicates the observations on the effect of air, the long dashes, those on nitrous oxide, and the short dashes, those on ethylene.

Since lumbar punctures on dogs are at best somewhat difficult, red blood cells were looked for as a routine in all specimens of spinal fluid before the hemolyzing agent was added, and when they were found allowance was made in the white blood cell count on the basis of 1

of the three gases, two animals receiving three successive injections, and the third animal four injections. The injections were performed in the routine manner already described. Roentgenograms were made to check the actual presence of the gas. In the animals receiving nitrous oxide and ethylene the three injections were performed on consecutive days, and in the animals in which four injections were made the series of three followed an initial injection a month earlier. These animals were killed on the first, second and third day, respectively, following the final injection. When air was used successive injections were carried out at weekly intervals, since the gas remained present so long and the three animals were killed on the first, second and fifth day, respectively, after the final injection. The dog listed as being killed on the first day following the third injection of air actually died with acute signs of increased intracranial pressure (slow pulse and respiratory rates) two hours after the final injection of air. Hypertonic solution of dextrose was administered intravenously without avail. Immediate autopsy revealed a bulging tense dura, flattened cortical convolutions and internal hydrocephalus, with obliteration of the normal lateral and third ventricles to form one large cavity in the middle of the brain. Hydrocephalus in this animal had been diagnosed by encephalography before death. In spite of this striking abnormality, the animal appeared normally intelligent and cooperative. However, in view of its abnormal condition, the death of this animal cannot be attributed, unreservedly, to encephalography carried out with air.<sup>49</sup>

The animals were killed by the intracardiac injection of air. The brain, meninges and cord were removed and fixed in Cajal's solution.<sup>50</sup> Sections were cut to show the frontal cortex, the cortex in the region of the sylvian fissure, the wall of the ventricle, the cerebellar cortex and the middle portion of the cervical and lumbar segments of the cord in each animal. Routine hematoxylin and eosin stains were made of all sections, and sections were stained by Hortega's silver carbonate method<sup>51</sup> and Cajal's gold chloride sublimate method<sup>51</sup> in a few instances in which questionable pathologic changes were noted.

The observations in each instance for all gases were within the limits of normal. Even in the dog that died following air encephalography hemorrhagic or inflammatory changes were not noted in the brain, cord or meninges.

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49 An intermittent block mechanism at the aqueduct of Sylvius seemed the most likely explanation to account for the old hydrocephalus, successful encephalography on two occasions and final acute block following the third injection of air.

50 The formula is: solution of formaldehyde 40 per cent, 300 cc, ammonium bromide, 40 Gm., and distilled water, 1,720 cc.

51 Penfield, W., and Cone, W. *Neuroglia and Microglia*, in McClung, C. E. *Handbook of Microscopical Technique*, New York, Paul B. Hoeber, Inc., 1929.

white blood cell for each 500 red blood cells per cubic millimeter.<sup>47</sup> Cell counts which were obscured by bloody taps were discarded except in two or three questionable instances, as indicated in the table, in which for the sake of an otherwise good series they were retained.

The effects of the final two injections in dog 66 (air and ethylene) appear abnormally prolonged (table 2), and, although the animal clinically seemed normal, it is possible that these last two injections stirred up a low grade meningitis sufficient to cause the abnormality noted in the cell count.

Since the number of punctures which can be performed satisfactorily in any one animal is limited, adequate comparative studies are difficult. This difficulty is increased by the fact that comparable injections of gas cannot be made as a routine and that—as may be determined

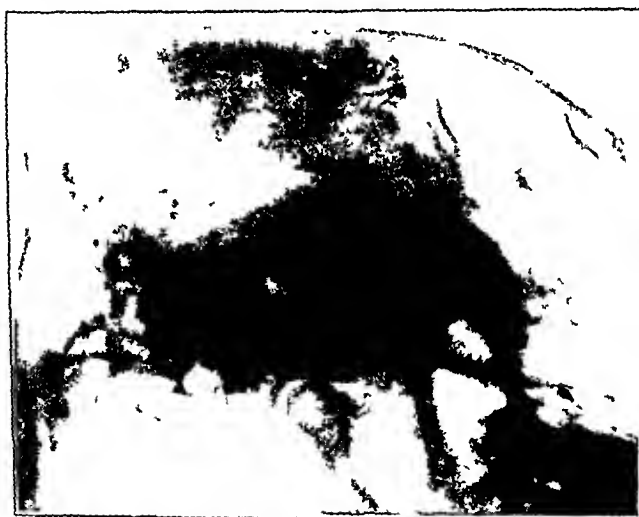


Fig. 3 (dog 42) —Slight ventricular filling with nitrous oxide

from the data presented in table 2, the cell reaction varies considerably with the degree of filling, regardless of the type of gas used. This is more clearly demonstrated in dog 42, in which different fillings of the same gas (nitrous oxide) corresponded roughly with the cell reactions produced. The roentgenograms in figures 3 and 4 may be compared with the corresponding total cell counts (table 2 and fig. 2). Only a large series of observations would overcome these difficulties and afford conclusive comparison.

The limited series presented, however, is of considerable interest in the comparison of comparable fillings (i. e., roughly equal as checked

<sup>47</sup> The blood count in the dog is essentially the same as that in man. The use of this ratio of 1 white blood cell per 500 red blood cells is supported by the recent work of Solomon, Darlev and Fremont-Smith (Contamination of Cerebro-spinal Fluid by Blood, *Arch. Neurol. & Psychiat.* **31** 1222 [June] 1934).



## COMMENT

It is interesting to correlate the effects obtained by the encephalographic injection of the gases used (table 1) with their known physical and physiologic properties (table 5). It may be seen, for instance that the time each gas remains in the ventricles roughly corresponds to its solubility. In a rough way, the combined factors of anesthetic power and solubility seem to be the factors which determine the narcotic effect of these gases following injection into the subarachnoid space. Thus, the weaker and more insoluble gases (acetylene, ethylene and nitrous oxide) have only a limited effect while the more potent and soluble anesthetics (ether, ethyl chloride and vinyl ether) cause profound and dangerous anesthesia.

Irritation and residual paresis might conceivably be associated with fat solubility, the more fat-soluble gases producing destructive changes at the site of injection. This correlation does not seem to be borne out, however, as may be seen in the effects of ether and di-vinyl ether as compared with those of ethylene and cyclopropane.

A rate of absorption faster than the elaboration of cerebrospinal fluid to replace the absorbed gas might conceivably produce an undesirable effect. Liberson<sup>50</sup> explained his unfavorable results with encephalography carried out with carbon dioxide in this way, i. e., as a too rapid absorption of carbon dioxide in the cerebrospinal fluid. With carbon dioxide, at least, other factors, such as possible disturbance of the acid-base equilibrium in the central nervous system or the convulsive reactions noted by Leake and Waters<sup>52</sup> with certain proportions of carbon dioxide and oxygen, should be considered.

In the present experimental work no such ill effects were observed. Spells of restlessness with whining and struggling followed some of the injections, particularly those of air and acetylene, but it is scarcely logical to attribute this to the rate of absorption, for although acetylene is one of the more rapidly absorbed gases, air is by far the most slowly absorbed. The known fairly rapid rate of formation of cerebrospinal fluid, as well as the lack of ill effects with constant drainage of the fluid, further argue against such a possibility.

It is interesting to note, in addition, that in water solubility both nitrous oxide and ethylene lie between carbon dioxide reported by Liberson to be too rapidly absorbed, and oxygen, which has been used successfully and has been found superior to air. Other common non-anesthetic gases which might conceivably be used for trial in this study have solubility rates approximately or less than that of oxygen. Such organic gases as ethane and methane, besides possessing questionable

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<sup>52</sup> Leake, C. D., and Waters, R. M. Anesthetic Properties of Carbon Dioxide, *Anesth & Analg* 8:17 (Jan-Feb) 1929.

by roentgenogram) of the same animal. Thus, in figures 4, 5 and 6 are shown roughly comparable fillings in dog 42, with nitrous oxide, ethylene and air, respectively. These may be compared with the corresponding total cell reaction shown in figure 2. An and nitrous oxide apparently produce about the same degrees of reaction in the cerebrospinal fluid and less than that produced by ethylene.

Another suggestive finding was the somewhat prolonged reaction to an, which corresponds with its known slower absorption. In four of five tests with nitrous oxide and in two of three tests with ethylene (the third being that in dog 66, which, as explained, should probably be discarded), the cell count had returned essentially to normal in seven



Fig 6 (dog 42) —Massive ventricular filling with air

days. With air, on the other hand, the counts remained slightly more elevated and did not reach normal for about ten or more days. This greater, prolonged reaction to air is even more apparent when comparable fillings in the same animal are studied. In table 2 and figure 2 are shown the total cell reactions to "massive" fillings of the various gases in dog 42.

The differences between the reactions of the cells following the injections of nitrous oxide in dog 45 by the lumbar and cisternal routes are interesting (tables 2 and 3). Slight ventricular fillings were obtained in both instances.

*Cytologic and Pressure Reaction of the Cerebrospinal Fluid to Cyclopropane and Oxygen*—Similar studies were made of the spinal fluid of three dogs which received injections of cyclopropane and of

# THE SURGICAL TECHNIC OF TOTAL PNEUMONECTOMY

WILLIAM FRANCIS RIENHOFF JR, MD

BALTIMORE

Since the publication two years ago of the operative technic employed in the total removal of the lung,<sup>1</sup> changes have been made from time to time not only in the actual surgical procedure but also in the preoperative preparation of the patient, in the method of administration and the type of anesthesia and in the postoperative care and observation. In this report only brief reference will be made to other than the actual surgical technic. It should be stated, at the outset, that the series of cases from which my impressions have been deduced, though relatively large, is actually small so that definite conclusions cannot be drawn at this time, and it is preferable that the experiences to be related should be regarded for the time being as suggestions, as the surgical treatment of diseases of the lung is still in its infancy. That total pneumonectomy has passed the stage of the purely imaginary and experimental must be admitted because of the number of such operations already successfully performed. Without exaggeration it may be stated that resection of an entire lung seems to be a feasible operation which has proved itself worthy of a place among the recognized, technically safe procedures. It might also be concluded that the immediate and remote mortality, as well as the postoperative incapacitation following this operation, will compare favorably with the results of surgical procedures employed for the eradication of tumors of the viscera elsewhere in the body.

The main objects of this paper are, first, to present for consideration certain improvements in the surgical technic of total removal of the lung and, second, to refer briefly to the preoperative preparation and the postoperative care of patients on whom total pneumonectomy has been performed.

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From the Department of Surgery of the Johns Hopkins University and Hospital

1 Rienhoff, W F, Jr. Pneumonectomy. A Preliminary Report of the Operative Technique in Two Successful Cases, *Bull Johns Hopkins Hosp* **53** 390 (Dec) 1933. Rienhoff, W F, Jr, and Broyles, E N. The Surgical Treatment of Carcinoma of the Bronchi and Lungs, *J A M A* **103** 1121 (Oct 13) 1934. Technique of Total Pneumonectomy and Lobectomy, *Proc Inter-State Post-Grad M Assembly North America*, 1934. Discussion on Archibald, E. Technique of Total Unilateral Pneumonectomy, *Tr Am Surg A* **52** 79, 1934.

TABLE 4—Comparative Study of Cell Count and Pressure of Cerebrospinal Fluid and Roentgen Observations Following Encephalography with Oxygen and Cyclopropane

TABLE 4—Comparative Study of Cell Count and Pressure Encephalography with Oxygen and Cyclopropane																				
	Dog 4, Cisternal Puncture Amytal Sedative			Dog 12, Lumbar Puncture Morphine Sedative			Dog 93, Cisternal Puncture Amytal Sedative													
	Differential Cell Count, Percent age			Differential Cell Count, Percent age			Differential Cell Count, Percent age													
Date	Total Cell Count			Total Cell Count			Total Cell Count													
	Poly morpho nucleurs	Lymphocytes	Monocytes	Poly morpho nucleurs	Lymphocytes	Monocytes	Poly morpho nucleurs	Lymphocytes	Monocytes											
6/13	2	0	100	0	100	0	0	0	100											
6/14	1 511	6	22	77	5	18	68	3	8											
6/16	1 132	3	64	20	33	70	25	2	50											
6/20	11	0	23	77	23	55	6	3	12											
Subarachnoid gas and massive ventricular filling			Subarachnoid gas and slight ventricular filling			Subarachnoid gas and food ventricular filling			Subarachnoid gas in cisternal Amytal Anesthesia											
Dog 267 Cisternal Puncture Amytal Sedative			Dog 361 Cisternal Puncture Amytal Sedative			Dog 12 Lumbar Puncture Amytal Sedative			Dog 93 Cisternal Puncture Amytal Anesthesia											
6/25	1	50	50	3	70	30	68	0	12	90	7/2	1	0	100	0	70				
6/26	1,750	80	1	1,155	78	12	10	85	14	80	5	6	100	75	11	14	55			
6/28	35	24	52	275	22	70	8	90	1,838	25	42	33	6	1,062	21	50	29	40		
7/2	14	17	33	41	0	67	31	90	7/2	6	23	70(?)	7/9	41	16	84	0	90		
Subarachnoid gas and massive ventricular filling			Subarachnoid gas and good ventricular filling			Subarachnoid gas in cisterna magna			Subarachnoid gas in cisternal and cortical areas											
Roentgen findings			Roentgen findings			Roentgen findings			Roentgen findings											
Oxygen			Oxygen			Oxygen			Oxygen											
Cerebrospinal fluid			Cerebrospinal fluid			Cerebrospinal fluid			Cerebrospinal fluid											
Roentgen findings			Roentgen findings			Roentgen findings			Roentgen findings											

at least to infect it to the extent that it will be invaded. As a result of this lining of granulation tissue, in the whole series of fifty-two cases not one instance has occurred of generalized empyema or invasion of the mediastinum producing so-called mediastinitis. Furthermore, the defense mechanism, having been mobilized before the soiling of the thoracic cavity occurs, provides for the phagocytosis of bacteria which have contaminated the field after the operation, so that the reconstructive fibinous exudate which precedes the formation of a space-occupying labyrinth of fibrous tissue is not destroyed by or with the formation of pus. In every case of this series there has been deposited a gelatinous plasma clot which fills the entire remaining dead space, and in those in which a compensatory dilatation of the opposite lung or lobes thereof has not occurred this fibinous mass has become organized and has served as a space-occupying fibrous tissue body which has obliterated the remaining unoccupied part of the thoracic cavity. The details of this type of preoperative preparation of the thoracic cavity and its advantages will appear in a later issue of the *Bulletin of the Johns Hopkins Hospital*.

#### SURGICAL TECHNIC

In previous communications attention was first directed to the obvious anatomic advantages of a high anterior approach over the hilus when total removal of the lung is contemplated. In the early cases of this series the surgical technic was carried out as described in the first reports, namely, by intrapleural dissection and individual ligation of the pulmonary artery and veins and closure of the bronchus. In the later cases, however, this technic has been somewhat changed and it is to this alteration that attention is especially directed, because it is a valuable adjuvant in facilitating the removal of the lung. The technic for the right and that for the left side are discussed individually. For the benefit of those not familiar with the anterior approach in contradistinction to the posterior approach, used previously to 1934, the entire surgical procedure is described in detail.

It was soon recognized that proper exposure of the lung could be obtained without resorting to the resection of ribs, and at the same time the length of the operation was shortened and postoperative convalescence was accelerated and ameliorated. In the entire series of thirty cases adequate exposure has been obtained by making an anterolateral incision in the third interspace (fig 1A) and then separating the ribs by means of a self-retaining retractor. It is to be noted that this incision may be made below the line of the nipple and should be carried from the parasternal line in front to the anterior axillary line laterally, if more exposure is desired, it can be continued posteriorly, but it has not been found necessary in this group of cases to exceed the

TABLE 5—Physical and Physiologic Properties of Gases\*

Gas	Formula	Specific Gravity†††	Boiling Point, C	Solubility‡	Partition Coefficient	Concentration of Anesthetics 50 to 60% in O <sub>2</sub> §
Acetylene	C <sub>2</sub> H <sub>2</sub>	0.90 (A)	-83.6	67.2 cc (W)§ 74.5 cc (W)§ 73.5 cc (W)§	64 #	15 to 20% in air** 3 to 9% in air†† 1 to 6% in air†† 1 to 9% in air§§
Cyclopropane	C <sub>3</sub> H <sub>6</sub>	1.16 (A)#	-33.4#	0.16 cc at 30 C (W)# 136 cc (N S)††	2.5±0.2 (at 20 C)§§ 2.3±0.1 (at 20 C)§§	87 to 88% in O <sub>2</sub>
Di vinyl oxide	(C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> O	0.81††	28.3††	1,234 cc (N S)	13.2#	92% in O <sub>2</sub>
Ether	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O	0.71#	34.5	2.3 cc (W)    500± cc (B)		0
Ethyl chloride	C <sub>2</sub> H <sub>5</sub> Cl	0.917 (A)	12.2	8.1 cc (W)   11.9 cc (W)§		6 to 12% in air##
Ethylene	C <sub>2</sub> H <sub>4</sub>	0.978 (A)	-103.8	33 cc (W)		
Nitrous oxide	N <sub>2</sub> O	1.53 (A)	-89.5	2.52 cc (W)		
Oxygen	O <sub>2</sub>	1.103 (A)	-182.7	(?) less than 100 cc (W)***		
Vinyl chloride	C <sub>2</sub> H <sub>3</sub> Cl	0.86	-13.6			

\* The data were obtained from Hodgman, C. D. Handbook of Chemistry and Physics, ed 17, Cleveland, Chemical Rubber Publishing Company, 1932, and otherwise according to the references noted.

††† Air (A) = 1.

‡ The solubility is represented by the number of cubic centimeters of gas required for the maintenance of anesthesia in blood, and N S, solubility in lipid (olive oil).

§ The partition coefficient equals solubility in water.

|| The concentration of the anesthetic is the percentage by volume required for the maintenance of anesthesia.

§§ Extrapolation is based on data on solubility from Seidell, A. Solubilities of Inorganic and Organic Compounds, ed 2, New York, D. Van Nostrand Company, 1933.

||| The gas was acetylene.

## Shipway, F. E. Acetylene, Ethylene, Propylene, Lancet 1 1126 (May 30) 1922.

\*\*\* Henderson and Johnston 1919.

† R. B. Ald.

†† Leake, O. D., and Chen, M. Y. Anesthetic Properties of Certain Unsaturated Ethers. Proc. Soc. Exper. Biol. & Med. 28 151 (Nov.) 1930.

§§ Leake, O. D., The Pharmacology of Ethyl Chloride, Proc. Roy. Soc., London, 5 B 78 391, 1906.

||| Imbley, E. H. The Pharmacology of Ethyl Chloride, The Macmillan Company, 1921.

## Gwathmey, I. T. Anesthetics, ed 2, New York, The Macmillan Company, 1921.

\*\*\* Gwathmey, I. T. Anesthetics, ed 2, New York, The Macmillan Company, 1921.

## Gwathmey, I. T. Anesthetics, ed 2, New York, The Macmillan Company, 1921.

\*\*\* Gwathmey, I. T. Anesthetics, ed 2, New York, The Macmillan Company, 1921.

costochondral junction will occur, but this has brought about no bad results either at the time or after operation. In each case in which separation had been caused, the reunion of the rib to the cartilage took place before the patient was discharged from the hospital. As shown in figure 1 *B*, the lung completely covers the hilus on its anterior and superior surfaces, coming in contact on both the right and the left side with the mediastinal pleura, and when this lappet, which overlies both the right and the left pulmonary artery, is freed and retracted, the first anterior or ventral branches of the artery are revealed (fig 1 *C*)

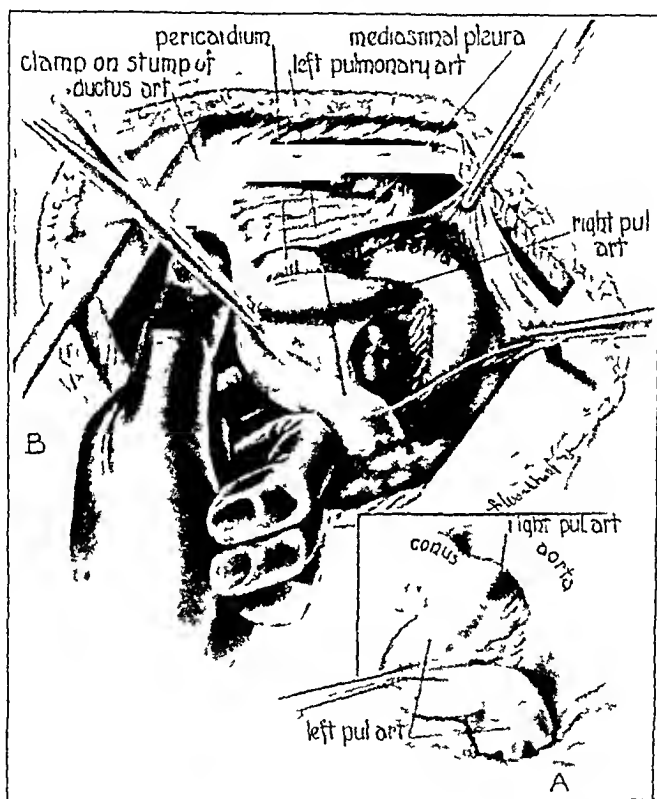


Fig 2—*A* is a diagrammatic sketch showing areolar tissue surrounding the posterior surface of the left pulmonary artery and the division of the pulmonary aorta into the right and left pulmonary arteries outside the pericardium. The first and second ventral branches of the left artery are also shown. *B* demonstrates reflection downward of the left pulmonary artery by gentle traction on the clamped stump of the ductus arteriosus. The point at which the obliterated strand is severed from the aorta can be seen as a small rough spot on the under-surface of the aortic arch. The index finger is passed under the left pulmonary artery with ease. Reflection of the pericardium is also shown.

*Resection of the Left Lung*—Particular attention is called to the fact that on the left side the intrapleural portion of the pulmonary artery is very short, indeed, it might be said that the branching of

toxic and narcotic properties also have about the same water solubility as oxygen. Thus, from the standpoint both of optimal absorptive rate and of safe sedative effect, nitrous oxide and ethylene stand out as the logical gases for trial in encephalography and ventriculography in man. This work, indeed, has already been started and will be the subject of a later report.

#### SUMMARY AND CONCLUSIONS

A satisfactory method has been developed for testing and comparing the effect in dogs of various gases used in encephalography.

Injections of air for control observations, have given results in dogs comparable in all respects to the results obtained clinically in human beings.

Ethyl chloride, di-vinyl chloride, ether vinyl chloride, and acetylene proved unsatisfactory for encephalographic use, the first three being decidedly dangerous.

In limited series the effects of oxygen and those of cyclopropane appeared to be comparable to each other and definitely superior to those of air.

Because of their safety, good roentgenographic results, minimal irritation, definite sedative effect and lack of ill effects either clinically or pathologically, nitrous oxide and ethylene seem ideal agents for encephalography.



rior, superior and posterior aspects of the primary bronchus. Its exceedingly short length between its emergence into the pleural cavity and the departure of those branches gives the operator very little room to free the main artery. The main point of danger is the dissection of the posterior surface of the artery from the anterior aspect of the bronchus, for it is here that the large posterior descending branch may be torn. Control of hemorrhage is also more difficult here than at any other point, because the vessels are literally entwined around the unyielding, stiff primary bronchus and can be clamped individually only by the greatest of good luck, the tip of the clamp usually grasping the rigid wall of the bronchus. When this happens, large amounts of tissue must be clamped and transfixed, and what might have been a methodical dissection is transformed into a rather crude amputation. Although apparently not generally appreciated, a much better exposure of the pulmonary artery on the left side may be obtained by incising the mediastinal pleura. As shown in figure 1 *C*, by using a blunt dissector the areolar tissue surrounding this portion of the pulmonary artery may be dissected away with ease. Running between the aorta and the superior surface of the left pulmonary artery, a small but well defined bundle of white glistening tissue may be observed, the fibrous strands of the obliterated ductus arteriosus (fig 1 *C*), which, when divided and clamped, provides an excellent retractor, freeing the pulmonary artery from its attachment to the aorta and allowing it to be pulled down and somewhat rotated (fig 2 *A* and *B*). In this way the posterior surface of the left artery is revealed for a distance of 2.5 cm. from the point at which the pulmonary artery divides into the right and left pulmonary arteries to the coming off of the large posterior branch.

It is to be especially noted that this space, which is the point of election at which to ligate the left pulmonary artery, in reality is extrapericardial and in the superior mediastinum. It is bounded above by the arch of the aorta, behind by the primary bronchus of the left lung and the portion of the pericardial sac covering the left auricle and below by the superior left pulmonary vein, and it is roofed over by a small portion of the redundancy of the superior reflection of the pericardial sac but in the main by the mediastinal pleura. It contains the terminal portion of the pulmonary artery and almost the entire left and the beginning of the right pulmonary artery, as well as the lymphatic glands which lie on the anterior and lateral surface of the primary bronchus of the left lung. It is elsewhere filled with loose areolar tissue. Dissection of this space permits of excellent exposure of the entire left pulmonary artery and its easy separation from the surrounding areolar tissue lying between it and the left primary bronchus posteriorly and the pericardial sac inferiorly. Occasionally a small opening may be made in the peri-

## MATERIAL

The series constituting the material from which this report is made is composed of ten cases in which total pneumonectomy has been performed and twenty others in which, because of the extent of the disease process, it was impossible to remove the whole lung. The latter group, however, provided many opportunities for the improvement of the surgical technic and for observation of the immediate results of certain procedures. Of the former group of ten cases in which complete pneumonectomy has been accomplished, in four the operation was performed on the right side and in six on the left. Eight of the ten patients were operated on for tumor of the lung and two for unilateral tuberculosis. In this group there has been one immediate operative death due to diffuse lobular pneumonia resulting fatally on the fifth day, three patients died later, one six months later of metastases to the brain, another after three months of tuberculosis of the remaining lung and the third six weeks after operation of pulmonary embolism. Excepting the patient who succumbed to tuberculosis, the other three died in the hospital, thus providing me with the opportunity to study the interesting intrathoracic anatomic readjustments, which could be compared with certain clinical findings, as well as a series of roentgenograms made at regular intervals until just before death. Of the remaining six patients who are alive, it has been possible to study the clinical course at frequent intervals because they are nearby residents of Baltimore.

## PREOPERATIVE PREPARATION

The preoperative preparation of the patient is of the greatest importance to insure stabilization of the pulse and blood pressure during the operation and successful primary healing of the bronchus, together with subsequent obliteration of the remaining dead space. The preparation consists, first, in producing if possible a complete collapse of the lung by gradually induced pneumothorax. In this manner the cardiorespiratory mechanism is stabilized, and the patient becomes accustomed to breathing with one lung. The main portion of the circulation through the pulmonary aorta is forced to pass through the contralateral rather than through the collapsed lung. This diminishes the possibility of circulatory disturbance following the immediate ligation of the pulmonary artery on the affected side and furthermore seems to prevent the shock associated with the opening of the pleural cavity because the patient has become used to an intrathoracic pressure slightly greater than atmospheric pressure. Thus, when the chest is opened at the time of operation there is no embarrassment from the effect of a temporary open pneumothorax. Second, for over two years it has been my custom to produce an inflammation of the parietal and visceral pleura in order to incite a serofibrinous pleurisy followed by the formation of granulation tissue. I have done this in the twenty-eight cases mentioned in this report and in twenty-four cases in which only partial pneumonectomy has been performed for bronchiectasis. As is well known, it is much more difficult, if at all possible to infect a granulating surface or

stump has been amputated, and the closure has been made with the epithelial surfaces abutting each other, just as occurs in the suturing of the intestine or of the surfaces of the skin. It may be that the difficulties in the past in dealing with a secondary opening of the bronchus were due to excessive traumatization from crushing, cauterization or widely spaced ligatures, with strangulation of the bronchial artery. Even in the patients with tuberculosis in whom the bronchus was divided healing was per primam. Probably it would be advantageous, not only from the standpoint of giving the tumor a wide margin but also from that of guaranteeing secure closure, to amputate the bronchus as high as feasible, near the bifurcation of the trachea, for unquestionably the granulating surface about the bronchus becomes more vigorous and abundant if the stump is in contact with the mediastinal areolar tissue and pleura. There are numerous lymphatic glands which lie

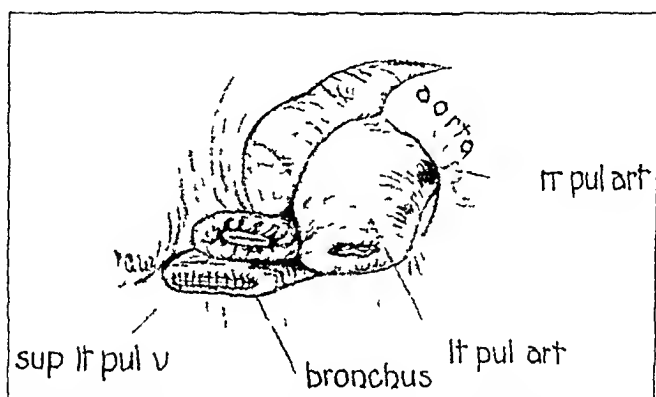


Fig 4—This diagrammatic sketch shows the stump of the hilum of the left lung, which has been dissected, with the vessels and the bronchus ligated individually. It will be noted that the bronchus is closed with interrupted silk sutures. This type of closure, with simple ligation of the artery and the vein, is considered the method of choice.

about the bronchus and can be removed only after an exploration of this space (fig 4).

*Resection of the Right Lung*—In total pneumonectomy on the right side, of which I have had four cases, the dissection is slightly different and somewhat more difficult than on the left side. The azygos vein is probably the best landmark for the beginning of the dissection. The mediastinal pleura is incised, and the areolar tissue separating the right pulmonary artery from the azygos vein superiorly, the superior vena cava anteriorly and the superior pulmonary vein and the posterior wall of the left auricle inferiorly is gently dissected (fig 5 B). The disposition of the branches of the pulmonary artery on the right side differ to some extent from that on the left. Running alongside of the epar-

limits previously described. The fibers of the pectoralis major muscle are divided along their course, and in only a few instances has it been found necessary to cut across them. However, this entails no difficulty or impairment of the postoperative function of the muscle. The incision in the internal intercostal muscles is made midway between the third and the fourth rib, so as to avoid the intercostal vessels, and the pleural cavity is opened as speedily as possible with practically no loss

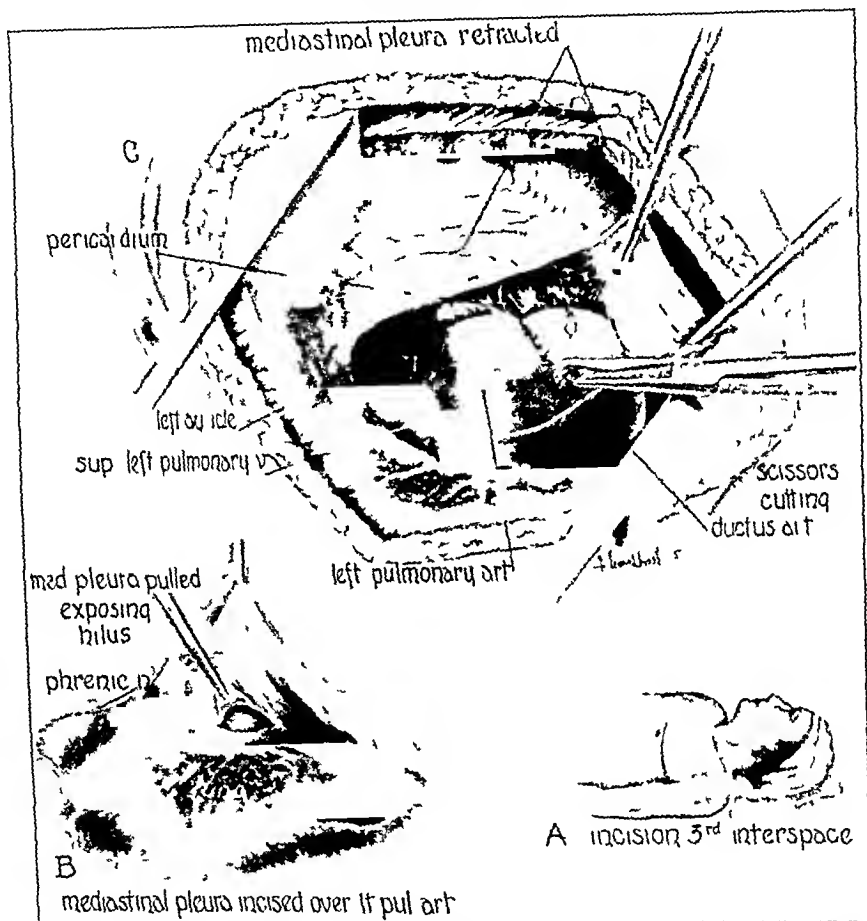


Fig 1—A shows the position of the patient on the table during pneumonectomy on the left side. An incision is made anteriorly in the third interspace. This position allows full expansion of the opposite lung. B shows exposure of the mediastinal surface of the upper lobe of the left lung. The anterior margin is laid back. The mediastinal pleura is incised, exposing the pulmonary artery. In C below the scissors may be seen the pleural mediastinal reflection. The pericardial reflection is shown as it blends with the mediastinal pleura after reflection off the systemic and pulmonary aortas.

of blood. It is surprising how extensive an exposure of the entire pleural cavity can be obtained by mere retraction of the third and fourth ribs. Occasionally disarticulation of the third or fourth rib at the

than the diameter of the main right pulmonary artery. However, with careful retraction of the superior vena cava (fig 5 C) and gentle separation of the inferior margin of the right pulmonary artery from the pulmonary vein and left auricle, the former may be mobilized proximal to its branches, and a ligature may be placed around it. The right pulmonary artery is, like the left, entirely extrapericardial, but it is longer than the latter because it passes across the entire mediastinum from the left to the right side. It has been the impression of many that the right vessel is shorter than the left and that both are intrapericardial. As on the left side, it is true on the right that if one dissects posteriorly it is perfectly safe, for there is nothing at these points posteriorly between the artery and the primary bronchi of the right and left lungs except areolar and lymphadenoid tissue, the latter of which, if a clean dissection is to be made, should be removed in any event. In my experience, the satisfaction of having the blood supply completely controlled in this manner has made the operation much easier, and the operator may then proceed with deliberation and confidence to the eradication of the mediastinal glands and the toilet of the bronchus, together with the freeing of any possible adhesions in the pleural cavity, and thus accomplish a complete removal of all the tissue of the lung together with the lymphatic vessels. This type of dissection has been followed out in my later cases, and in only one has the dissection been difficult. In this case the patient had received a great deal of external radiation, and the fascial cleavage between the right pulmonary artery and the surrounding structures was heavily scarred. Although it may be possible in some instances to remove the lung by placing mass ligatures around the hilus without dissecting out the vessels, in many instances the tissue of the lung that is left in such an unscientific procedure will already have been invaded by the malignant tumor, and a recurrence is certain.

In the removal of a lung it would seem that the same surgical principles should be observed as those followed in the radical operation for removal of carcinoma of the breast. The two procedures are certainly similar. In removal of the breast the vessels are dissected out in a meticulous manner, and the contents of the axilla are entirely removed. This operation has become, one might say, almost standardized throughout the entire world, and it is hardly too much to predict that the same type of careful dissection of the hilus, with removal of the adjacent mediastinal glands, will be the procedure of choice in cases of malignant tumor of the lung and that the same standardization will prevail wherever this type of surgical work is done as has been adopted in the surgical treatment of malignant disease of the breast. Certainly it must be admitted that the same hazards of an ultimate cure confront the operator in dealing with malignant tumor of the lung that are present

the left pulmonary artery occurs almost immediately on its entrance into the pleural cavity. Three large anterior branches emerge to supply the upper, middle and lower portions of the superior lobe of the left lung (fig 3 *A* and *C*), while coursing below and immediately behind the primary bronchus is the large posterior branch. This vessel is difficult to expose and because of its relatively thin wall is very easily and unwittingly torn. The artery fans out, as it were, so that its large posterior and smaller anterior branches intimately embrace the ante-

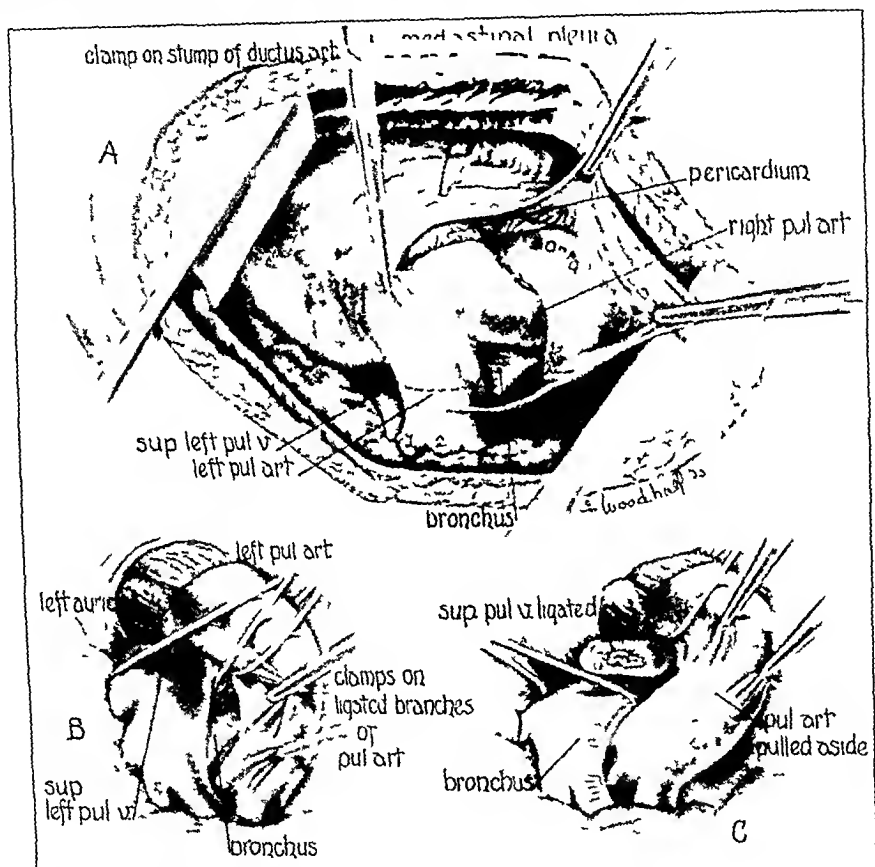


Fig 3—In *A* the suprapericardial mediastinal space described in the text is well defined by the arch of the aorta, reflection of the pericardium, the bronchus posteriorly and the superior left pulmonary vein. The dotted line shows the point of election for ligation of the artery. The intimate association of the two anterior and the large posterior branches of the left pulmonary artery with the bronchus is demonstrated. *B* shows the point of extrapericardial ligation of the superior left pulmonary vein and artery, indicated by the tapes. Clamps have been placed on the anterior branches (1 and 2) to demonstrate the distribution of the large posterior branch in its relation to the left primary bronchus. The departure of the first branch from the large posterior one is shown. *C* shows the superior pulmonary vein ligated, exposing the bronchus. The tape marks the level at which the bronchus should be divided. This point is within the extrapericardial mediastinal space. The pulmonary artery is further pulled aside, demonstrating the breaking up of the posterior branch into the first two smaller divisions.

result of direct trauma or the indirect effects of local inflammation. These factors tend to break down the protective mechanism of the patient. It was evident in one case, in which total pneumonectomy on the right side was carried out on Nov. 1, 1934, that excessive traumatization from an unskilful insertion of the tube resulted in traumatic tracheitis, which later developed into confluent lobular pneumonia of the remaining lung and resulted in the death of the patient. Tracheal râles were audible in this patient by the end of the operation, in spite of repeated attempts to aspirate material in the trachea. One of the early patients, she was placed in a modified Fowler position after operation, which allowed mucopurulent material to drain into the remaining good lung. The subsequent clinical course and findings led me to believe that had the patient not undergone the original traumatization of the trachea and had she not been left in a semisitting position the pneumonia might have been prevented. Another practice which I have given up, which at first seemed to be of value was the distention of the lung immediately after the operation, particularly after partial pneumonectomy, before the thoracic cavity was closed. I have since abandoned this procedure because I believe that organisms might be forced into the bronchial tree or even into the alveolar ducts and in that way might induce pneumonia. Unquestionably, the more simple the administration of the anesthetic the less the danger, and it is my opinion that, except in cases of suppurating infection in which aspiration may be necessary, it would be better not to introduce an intratracheal tube.

#### POSTOPERATIVE PROCEDURES

The position of the patient in bed after operation is of prime importance in preventing respiratory complications. It is advisable to adopt the Trendelenberg position, with the foot of the bed elevated for the twenty-four hours following the operation, thus producing free bronchial and tracheal drainage with the minimum effort on the part of the patient. This position creates a tendency for mucus to drain toward the pharynx rather than toward the tissues of the remaining lung. Moreover, the patient is placed on the side operated on, so that there will be no restriction in the respiratory excursion of the side not operated on, and thus the maximum exchange of air may be accomplished with a minimum of effort. Again, keeping the side not operated on in the elevated position favors bronchial drainage away from the alveoli toward the primary bronchus. An oxygen tent is used as a routine for the first twenty-four to forty-eight hours in order to minimize still further the respiratory efforts and to keep the blood well oxygenated. Often, as the result of a tight dressing or because the patient is allowed to lie in a semisitting posture on the side opposite that operated on,

cardial reflexion, but this can be closed very easily. The separation of the left pulmonary artery in this space is much more easy of accomplishment than dissection of the artery in the space of 0.5 cm. in which it lies free in the pleural cavity. Particularly is this true if a tumor is involving the hilus of the lung or extends high up into the bronchus. These circumstances often render it physically impossible to ligate the pulmonary artery intrapleurally and therefore leave the surgeon unable to cope technically with an otherwise operable condition. For in such a circumstance he is almost sure to tear either directly into the artery or into one of its branches. As there are no branches within this mediastinal space, the operator has only to separate gently the areolar tissue between the artery and its surrounding structures such as the aorta, the bronchus and the superior posterior portion of the pericardial sac. In some instances this has been accomplished by a gentle maneuvering of the index finger, so delicate is this areolar tissue (fig. 2B).

The pulmonary artery divides just outside the pericardial sac about 1.5 cm. proximal to the stump of the obliterated ductus arteriosus and in this suprapericardial mediastinal space may be seen the beginning of the right pulmonary artery. After ligation of the left pulmonary artery the mediastinal pleura may be closed. The superior and inferior pulmonary veins can then be dealt with in the order named, as they are easily ligated within the pleural cavity, for the branches of both the superior and the inferior vein converge before they pass into the pericardial sac. In the space on the left side the bronchus also is easily exposed, and a high amputation is therefore made possible. In this series of cases the closure of the bronchus has not been difficult or disappointing. The method employed has been as simple as possible, the closure of the bronchus being carried out in accordance with the general surgical principles that would apply to closing an incision in the skin. The cartilaginous ring is clipped circumferentially, and the bronchus is either ligated with an encircling ligature of double medium silk or sutured with interrupted double medium silk sutures. In only two of the ten cases have I experienced the slightest difficulty from the treatment of the bronchial stump and this occurred in the second and fourth cases. In these cases a small opening appeared in the bronchus of the left lung connecting it with a walled-off cavity which has persisted for over two years but has not caused the slightest embarrassment to the patient. In both of these cases the bronchus was closed well out in the pleural cavity and therefore depended on its own feeble granulation tissue for healing. In the later cases the bronchus has been ligated within the mediastinal space previously described where the more vigorous granulation tissue of the surrounding areola is of undoubted value in the promotion of healing. No cauterization either with the actual or with the chemical cautery has been resorted to. The bronchial



# PATHOLOGIC AND BIOCHEMICAL CHANGES IN SKELETAL DYSTROPHIES

## ANALYSIS OF RESULTS OF TREATMENT OF PARATHYROID OSTEOSIS

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An accurate interpretation of changes in the body associated with demineralization of the skeleton is dependent on knowledge of the metabolism of the mineral elements which are essential to the formation and function of bone.

The bony skeleton of the human body is more than a supporting structure. It is a reservoir or storehouse of calcium and phosphorus. Bone is not an inanimate substance comparable to a block of stone or a column of cement. It is a living tissue made rigid enough to support the body by the calcium carbonate and phosphate salts biologically laid down in it. In the adult as well as in the child these bone salts are continuously removed and renewed, so that there are a constant flow of both calcium and phosphorus away from the bones into the body fluids and a redeposition of similar salts, which have been absorbed from the intestinal tract.

Calcium is an element essential to the life of plants and animals. In several forms, usually in combination with phosphorus, which may be spoken of as phosphate of lime, it forms the principal constituent of bone. The dried skeleton of the adult human body weighs about 10 pounds (4.5 Kg). Approximately 5 pounds (2.3 Kg), or one half of this weight is composed of calcium salts and most of the rest is organic material consisting of dead cells and their fibrous projections, which form a fine meshwork in which the bone salts have been deposited by the cells.

Man derives calcium principally from milk, cheese, butter, eggs, green vegetables and nuts. When the various components of the adult body are functioning normally approximately the same amount of calcium is absorbed from the food in the intestines and so reaches the bones by way of the blood stream as that which is taken from the bones and lost to the body in the urine and waste material of the lower part of the bowel.

Various factors influence this process of absorption, deposition, reabsorption and excretion or loss of calcium. Vitamin D, which is present

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terial bronchus on the right side is the first ventral or anterior branch, while occasionally, a second anterior branch supplies the lower portion of the upper lobe of the right lung, after which comes the slightly more deeply situated branch to the middle lobe (fig 5 C). The tributaries to the superior pulmonary vein overlie the latter branch as well as the large posterior division of the artery, which is by far the largest of the four. However, on division of the superior pulmonary vein, which can be ligated with ease intrapleurally, the large posterior branch of the right pulmonary artery is exposed (fig 5 C). The difficulty of making an intrapleural ligation of the right pulmonary artery is at once appar-

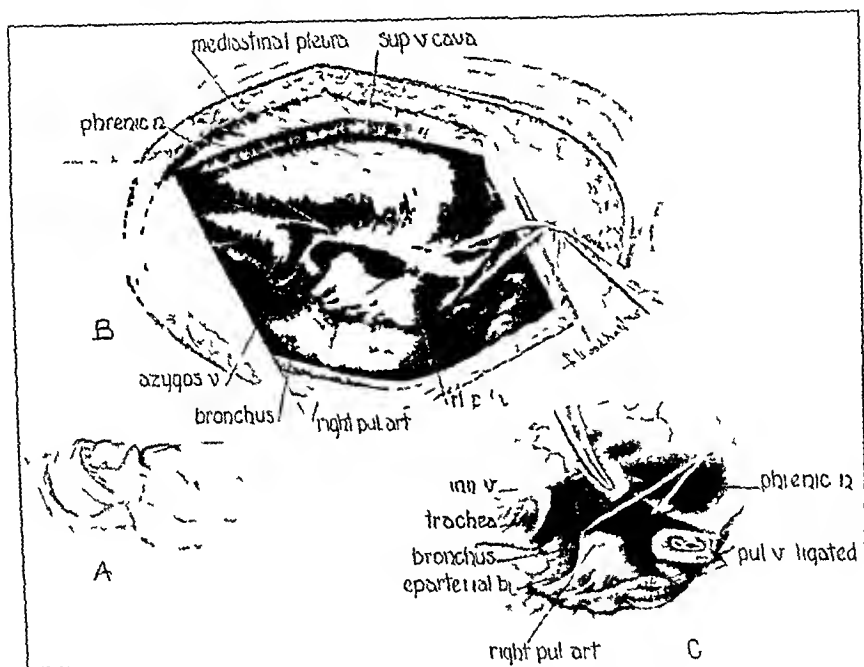


Fig 5—A demonstrates the position of the patient on the table during pneumonectomy on the right side. An incision is made anteriorly in the third interspace. B shows self-retaining retractors spreading the third and the fourth rib apart. The mediastinal pleura has been incised, and the right pulmonary artery and the right superior pulmonary vein are exposed. The azygos vein is shown at the level of the bifurcation of the trachea. The right primary bronchus is seen just below the azygos vein. In C the superior pulmonary vein is ligated, exposing the first two ventral or anterior branches of the right pulmonary artery and the large descending posterior branch. The tape is around the artery at the point of election for ligation. Areolar tissue surrounding the pulmonary artery has been gently removed by blunt dissection, freeing the artery from the primary bronchus posteriorly, the azygos vein superiorly, the superior vena cava anteriorly and the pulmonary vein inferiorly. A Kuttner dissector is shown freeing the superior vena cava from the right pulmonary artery.

ent, for the distance between the inferior margin of the descending branch and the superior margin of the first ventral branch is greater

parathyroid glands, and the two distinct entities are still confused by some writers as subtypes of a common form of fibrocystic osteitis

Von Recklinghausen, in a *Festschrift* to Virchow, also described cases of osteomalacia and osteitis deformans and 2 cases of generalized fibrocystic disease, he obviously considered all of the cases to be instances of slightly different manifestations of the same pathologic entity. Although the skeletal changes in similar cases had been described



Fig 1—Photograph of the skeleton in one of the cases first described by Recklinghausen. The multiple cystlike expansions of the bones and the many fractures and deformities are evident.

long before this time by Stansky and Engel, the condition of generalized osteitis fibrosa (parathyroid osteosis) is still spoken of as Recklinghausen's disease (fig 1).

Askanazy described a case of generalized osteitis fibrosa in which a tumor of the parathyroids was noted at necropsy. Although his diagnosis of the skeletal changes was "osteitis deformans," the description of the conditions noted at necropsy indicates that it should have been osteitis fibrosa generalisata or parathyroid osteosis.

with corresponding growths in the breast. Again, in both the breast and the lung it is possible to remove the entire organ together with its draining lymphatics. Hence, it would appear that a complete scrupulous dissection, which is admitted to be necessary for the former, is equally important for the latter. Few, if any, viscera in the body can be removed in their entirety with as little incapacitation of the patient following surgical intervention as in the case of the lung. If, as it would seem, resection of the lung is a feasible operation, with results comparable in immediate and remote mortality as well as in postoperative incapacitation to similar operations elsewhere in the body then to give it a place among other recognized technical, safe and worth while surgical procedures the operation must include a careful meticulous dissection of the hilus and its lymphatics.

*Closure of the Wound*—In this series of cases it has not been necessary to perform a thoracoplasty, even when pronounced displacements of the mediastinal vessels had occurred. Closure of the wall of the chest has been very simple. Three pericostal braided silk sutures are placed through the second and fourth interspaces and encircle the third and fourth ribs. The latter are then held together by a rib approximator while the sutures are tied. The overlying pectoral muscle and fascia are brought together with interrupted silk sutures. The skin is closed in a similar manner. Drainage of the thoracic cavity is not resorted to, because the accumulation of serum and plasma associated with the later formation of an obliterating fibrinous clot is desirable. If the patient has been properly prepared and the surgical technic has been good there should be no necessity for drainage.

#### TYPE OF ANESTHETIC AND ITS ADMINISTRATION

In all these cases tri-brom-ethanol in amylene hydrate was used, the dosage being 80 mg per kilogram of body weight, by rectum. This basal anesthetic was supplemented with nitrous oxide and oxygen, given, except in two cases, without an intratracheal tube. A high percentage of oxygen was used during the operation, with a small percentage of nitrous oxide. The anesthesia was very light, and the movements of the diaphragm and mediastinum after one had become accustomed to the rhythm were of no great inconvenience. Whether or not an intratracheal tube should be used is still an unsettled question. It cannot be denied that the insertion of a tube through the mouth into the trachea must always carry organisms into an otherwise sterile region, for it is certainly probable that in the uninfected patients with tumors of the lung the trachea is sterile. Furthermore, traumatization of the mucosa of the trachea caused by the tube would produce a mucopurulent exudate and at the same time interfere with the movements of cilia as the

the gross or the microscopic picture of bone involved by Recklinghausen's disease and that presented by a section of bone in a case of Paget's disease. The clinical picture of several of the abnormal skeletal conditions mentioned may be similar to that of generalized osteitis fibrosa (Recklinghausen's disease), which I prefer to call parathyroid osteosis. But while these diseases are clinically, roentgenologically and pathologically somewhat similar, there is a difference in the biochemical manifestations, as demonstrated in studies of the mineral metabolism. Parathyroid osteosis is characterized by a high calcium content of the serum, a low percentage of phosphates in the plasma, an increased excretion of calcium in the urine and a negative calcium balance.

#### ANALYSIS OF THE REPORTED CASES OF PARATHYROID OSTEOSIS

A study of the cases of parathyroid osteosis described since the report of Mandl shows that an adenomatous tumor of one or more parathyroid glands has always been observed at postmortem examination and nearly always at operation. Table 1 gives an analysis of 75 reported cases of generalized fibrocystic disease in which significant clinical data were reported and one or more tumors of the parathyroids were removed at operation. A more detailed analysis of these proved cases of parathyroid osteosis is shown in table 10.

The cases listed in table 2 were reported independently by other investigators, and they are also included in table 1. Data in the more detailed analyses of these cases presented in table 10 were obtained from a study of the reports of all the authors.

The analyses of 30 cases of parathyroid osteosis in which it was reported that adenomas of one or more parathyroid glands were observed at operation are included in table 3. Ballin reported successful operation in 22 cases of generalized osteitis fibrosa, but protocols of his cases have not been published. The clinical data on the other cases listed in this table are not sufficient to substantiate the diagnosis, although the reported discovery of adenoma of the parathyroids at operation indicates that the clinical diagnosis of parathyroid osteosis was confirmed.

With the exclusion of 1 duplicate, 8 cases are listed in table 4 in which a diagnosis of hyperparathyroidism was made but no tumor was observed at operation. Improvement was reported after removal of one or more normal glands in the cases of Cooley, Hannon, Shorr, McClellan and DuBois, Hitzrot and Comroe, and Landon. The youngest patient with a condition diagnosed as hyperparathyroidism to be subjected to operation for this disease was one of Landon's, a boy aged  $2\frac{1}{2}$  years. Roentgenograms and data on this case were submitted to consulting physicians, including Dr. Fuller Albright, who concurred in the diagnosis. That tetany did not follow excision of three normal

serious anoxemia develops insidiously, hence, every effort should be made to give perfect freedom to the side not operated on. It is not necessary to put on a tight dressing with a large mass of adhesive plaster wrapped around the wall of the chest. Another advantage of keeping the patient in the Trendelenberg position is that the clot of plasma which formed in all my cases was more or less evenly distributed throughout the empty space and was as abundant at the apex as at the base. This even distribution is desirable because it supplies a covering of the raw surface at the hilus of the lung with a fibinous clot that goes on rapidly to organization, and thus undoubtedly expedites the closure of the bronchus and insures at least a complete walling off of this region from the cavity that remains.

No drainage has been employed, nor has thoracentesis been necessary, in the cases of total pneumonectomy. The accumulation of plasma is looked on as a desirable feature, and the less it is disturbed the more rapid will be the deposition of fibrin with its subsequent organization. After forty-eight hours the patient can be put in a semisitting posture, but he should never be kept in one position throughout the twenty-four hours. The elevation of the bed and the position of the patient in the bed should be changed every two hours during the day and night.

Since it is only by the relation of the experience of those particularly interested in this field and by a full discussion of the results that one may hope to make constant improvements in one's methods, it is with this object in view that this report is offered.

TABLE 1—*Results of Removal of Enlarged Parathyroid Glands (Adenoma) in Cases of Osteitis Fibrosa Generalisata (Parathyroid Osteosis)—Continued*

Author	Sex	Age, Years	Result of Operation	Period of Observation after Operation
B Additional Cases Reported Since 1933				
1 Abel, Thomson and Hawksley	F	58	Improvement	12 months
2 Albright, Aub and Bauer	M	52		
3 Dyke, Walker and Freeman	F	14	Free from pain	
4 Dyke, Walker and Freeman	F	14	No change	
5 Dresser	F	44	Patient symptomatically well	
6 Dresser	M	15	Improvement	3 months
7 Gutman, Swenson and Parsons	M	31	Improvement	8 months
8 Gutman, Swenson and Parsons	F	53	Improvement	20 months
9 Gutman, Swenson and Parsons	F	35	Death	
10 Keynes and Taylor	M	26	Improvement	
11 Lewis and Trimble	F	67	Improvement	
12 Morelle	F	51	Improvement	1 month
13 Morton	F	21	Improvement	1 month
14 Schwensen and Iken	F	36		

\* This case is the one reported by Du Bois, in which operation was performed subsequently by Richardson with removal of two normal parathyroid glands. After repeated unsuccessful operations on the neck, Churchill explored the mediastinum and there discovered and removed a large adenoma of the parathyroid. The patient subsequently died of renal insufficiency. A number of these cases were reported independently by other authors. Some duplicates are listed in table 2.

TABLE 2—*Cases Included in Table 1 But Reported Independently by Other Authors\**

Author	Sex	Age, Years	Result	Time Elapsed after Operation	Authors Reporting Cases in Table 1
1 Albright, Aub and Bauer					Churchill and Cope (11 cases)
2 Amberg	F	14	Improvement		Pemberton and Geddie
3 Barrenseheen and Gold			No improvement	1 year	Gold
4 Bauer, Albright and Aub	M	30			Churchill and Cope also by Hannon et al
5 Brown	M	38			Barr, Bulger and Dixon (case 2)
6 Bulger, Dixon, Barr and Schregardus					Barr and Bulger (case 1)
7 Eftinger and Magendantz	M	33			Churchill and Cope and others
8 Hannon, Shorr, McClellan and Du Bois					Churchill and Cope also by Bauer, Albright and Aub
9 Petren, Ask Upmark	F	43	Death	20 days	Ask Upmark
10 Richardson, Aub and Bauer					Churchill and Cope and others (same as cases 3 and 6 in col 1)
11 Rankin and Priestley (case 1)					Wilder also by Weilbrock

\* There have been duplicate or multiple reports of other cases, but those included in this table have been listed to emphasize the fact that they should not be counted again in tabulating the total number of cases in the literature.

in cod liver oil, butter and a number of other oily substances and also in the skin of the body in an inactive form, is important in the absorption and deposition of calcium salts. Ultraviolet radiation from the sun or similar radiation from therapeutic lamps activates the sterols, which are normally present in the skin in large quantities, and liberates vitamin D. The absence of a sufficient amount of this vitamin in the diet and of sufficient sunlight or other sources of ultraviolet irradiation of the cutaneous surfaces of the body results in failure of absorption and deposition of sufficient bone salts. In the growing child this deficiency is characterized by weak bones which bend easily, producing a condition known as rickets.

The secretion or hormone of the parathyroid glands plays an important rôle in the metabolism of calcium and phosphorus. Experimental evidence offered by Johnson and Wilder and confirmed by Jaffe and Bodansky indicates that vitamin D either acts on the parathyroid glands to stimulate a greater secretion of the hormone or in some other way aids this hormone in the mobilization of calcium from the skeleton. The continued administration of parathyroid extract to young puppies, guinea-pigs or rabbits leads to generalized fibrous changes in the bones identical with the clinical condition which has been recognized by the name of generalized osteitis fibrosa or osteodystrophia fibrosa (Jaffe and Bodansky, and Johnson and Wilder) and more recently by a better descriptive term, suggested by Lievie, parathyroid osteosis. In experimental hyperparathyroidism the changes in the bones are more marked if viosterol is given in conjunction with the parathyroid extract.

The work of Robison and Kay and their collaborators has shown that an enzyme called phosphatase also has a part in the formation and physiologic action of bone.

#### HISTORY OF GENERALIZED SKELETAL DYSTROPHY

Denninger has described the skeleton of an American Indian from a burial-mound in northern Illinois of about 1,000 A.D. The lesions of these bones were considered to be those of generalized osteitis fibrosa. Until the latter part of the nineteenth century no distinction was made between the diseases characterized by softening of the bones, and all the disorders were classified under the term "osteomalacia."

In 1839 Stansky described in detail the study of a malacic skeleton from which most osseous elements had been lost and replaced by cysts and reddish tumors. Engel described a similar case in 1864.

A chronic inflammatory disease of the bones described by Paget is still recognized by his name or by the descriptive term osteitis deformans. Unfortunately, this disease was confused with the generalized fibro-cystic disease which is recognized to be due to tumor or tumors of the



Of 14 cases included in table 6, those of Christeller, Duken and Toennissen and von Hecker may be classified as presenting adequate data to justify the diagnosis of parathyroid osteosis

In 4 of 10 cases in which the diagnosis was parathyroid osteosis and the patient was subjected to roentgen irradiation over the thyro-

TABLE 5—Nine Cases of Hyperparathyroidism in Which No Tumor Was Seen at Operation and No Normal Glands Were Removed

	Author	Sex	Age, yrs	Comment
1	Bull	M	50	Condition unchanged subtotal thyroidectomy no parathyroid tissue noted
2	Bergmann			No tumor noted
3	Compere and Phemister	F	6	Nodule removed proved to be tissue of the thyroid gland
4	Dresser	F	35	No tumor noted irradiation later but no improvement
5	Elmslie et al	F	26	No improvement, regional osteitis fibrosa (?)
6	Terebinskij	F	2	No parathyroid tissue removed but small nodule of colloid thyroid tissue excised
7	Wendel (case 1)	F	20	No definite improvement tumor removed proved to consist of colloid thyroid tissue
8	Winter	F	12	
9	Wood	M		No tumor noted clinical diagnosis hyperthyroidism

TABLE 6—Cases in Which the Clinical Diagnosis of Hyperparathyroidism Was Made and No Operation Was Performed

	Author	Sex	Age, yrs	Comment
1	Barr and Bulger	F	11	Evidence not sufficient to justify presumptive diagnosis of hyperparathyroidism, blood chemistry normal
2	Barr and Bulger	F	24	Probably regional osteitis fibrosa
3	Bradfield	M	13	Mineral metabolism reported normal
4	Christeller	F	49	Calcium content of the serum from 14 to 17 mg
5	Duken	F	7	Diagnosis of advanced rickets and osteodystrophia fibrosa
6	Duken	F	14	Same diagnosis as in preceding case palpable tumor in the neck
7	Giordano	F	23	Data lacking
8	Giordano	M	48	Data lacking
9	Kleinboeck and Morkovitz			Possibly Paget's disease
10	Ortenberg	M	59	Probably Paget's disease, calcium and phosphorus contents normal
11	Regnier	F	48	Reported improvement from administration of viosterol
12	Tavener	F	53	No studies of mineral metabolism
13	Toennissen and von Hecker	F	52	Calcium content, 16 mg, bilateral renal calculi
14	Young and Cooperman	F	21	Inadequate data no suspicion of parathyroid tumor

parathyroid glands, definite improvement or cure was reported. This improvement included the healing of cystlike areas in the femur in the case of Merritt and of similar areas in the mandible in Hellstrom's case. No report of subsequent observation was given by Chabe. Biedl reported on experimental studies in which he irradiated the parathyroid glands

Erdheim described 3 cases of osteomalacia associated with enlargement of the parathyroid glands. He expressed the belief that the enlargement of the glands was due to simple hypertrophy or hyperplasia and was part of a compensatory mechanism to offset the loss of calcium. The results of recent studies of Wilde, Bauer and others indicate that the type of osteomalacia in the adult that is due to deficiency of mineral and vitamin in the diet is the equivalent of rickets and that the enlargement of the parathyroids in such cases may be, as Erdheim suggested, compensatory hyperplasia.

While studying a case of osteitis fibrosa cystica, Schlagenhauser recommended the removal of double palpable tumors of the parathyroid glands. Maresch, one of his associates, concurred in this opinion, but J. Bauer, the surgeon who was responsible for the results in the case, rejected the suggestion as too radical and dangerous. Mandl, however, was possessed of a more adventurous spirit. In 1925 he attempted to apply Erdheim's theory in a case of multiple fibrocystic disease. Four parathyroid glands taken immediately after death from the victim of an accident were successfully transplanted in the abdominal wall of a man, aged 38, with generalized osteitis fibrosa, but the disability became definitely worse after the transplantation. Mandl then decided that the aforementioned enlargement of the parathyroid glands in cases of similar skeletal conditions might be a cause and not a result of the changes in the bones. In an exploratory operation he observed a tumor behind the left lobe of the thyroid gland and excised it, and at the same time he removed the parathyroid glands which had been transplanted to the abdomen. The tumor proved to be an adenoma of a parathyroid gland, and after its removal the condition of the patient steadily improved.

From the studies of Mandl, Barr, Bulger and Dixon, Boyd, Milgram and Stearns, Hunter, and Churchill and Cope, and the investigations which my associates and I have made in this clinic, in which the diagnosis was confirmed in 124 cases by observation of tumor of the parathyroids at operation or at necropsy, parathyroid osteosis can now be defined as a definite clinical syndrome. This type of osteodystrophy is due to hyperparathyroidism associated with an adenomatous tumor of one or more of the parathyroid glands. It is a chronic disease, which progresses with pain, fractures and disabling deformities, and the outcome may be fatal. There is generalized demineralization of the bones of the skeleton and multiple foci of osteitis fibrosa, with or without benign giant cell tumors and cysts, are common. It is a disease entity differing from local or regional osteitis fibrosa, osteitis deformans, osteogenesis imperfecta, osteomalacia, rickets and ankylosing polyarthritis. The similarity in the roentgenographic findings of several conditions in this group is well known and the most experienced pathologist may at times find it difficult to differentiate between

In table 8 are included the cases of adenoma of the parathyroid glands discovered at necropsy during the years since Mandl reported the removal of a tumor of this type at operation in a case of multiple fibrocystic disease (An exception is the case of Dawson and Struthers, reported in 1923) In 19 of the 21 cases the diagnosis of the skeletal pathologic condition was generalized fibrocystic disease, but in 1 case studied by Hadfield and Rogers there were no changes in the bones, while the other exception was a case of acromegaly The association of parathyroid tumor and acromegaly will be referred to in another section of this paper The reports of the necropsy were not complete in all the cases referred to in the table, but in 6 either calculi or deposits of calcium in the kidneys were mentioned

A review of the symptoms of the patients reported on by various writers and the observations at examination reveals a number of similar conditions All the patients whose histories were given complained of

TABLE 9—*Summary of Data in Cases of Parathyroid Osteosis*

Data	No. of Cases
Adequate clinical data, adenoma observed at operation	75
Inadequate data, adenoma reported at operation (cases of Schimbel and von Dique discarded as possible duplicates)	23
Clinical diagnosis, no tumor seen at operation, but one or more normal glands removed	8
No tumor noted, no glands removed	8
Diagnosis of fibrocystic disease which was thought to be due to parathyroid adenoma, no operation performed to seek the tumor (cases not counted in which data were incomplete or diagnosis was doubtful)	4
Treatment by roentgen irradiation	9
Clinical diagnosis but parathyroid tumor observed only at autopsy	21
Total number of cases of parathyroid osteosis studied	153

progressive muscular weakness, pain in or bowing of the weight-bearing extremities and general lassitude But in the case of Chievitz and Olsen there was no hypotonia or decrease in muscular irritability In all the patients osteoporosis of the bones of the skeleton was noted

#### OSTEOMALACIA AND RICKETS

The mere recognition of osteoporosis of the human skeleton associated with hypotonia and decreased irritability of the muscles to electrical stimuli, with or without elevation of the calcium content of the serum, is too little evidence on which to base a diagnosis of overfunction of the parathyroid glands The presence of enlarged parathyroid glands in the absence of a negative, or at least a reduced, calcium balance does not justify the removal of the glands Hyperplasia of the parathyroid glands may be a purely compensatory enlargement in response to a demand of the organism resulting from deficiency in the absorption of calcium from the bowel This has been demonstrated clinically in cases of deficiency diseases such as osteomalacia and rickets by Hoffheimz

TABLE 1—Results of Removal of Enlarged Parathyroid Glands (Adenoma) in Cases of Osteitis Fibrosa Generalisata (Parathyroid Osteosis)

Author	Sex	Age, Years		Result of Operation	Period of Observation after Operation
		A	Sixty One Cases		
1 Allen and Camp		?	Improvement	10 months	
2 Ask Upmark	F	43	Death	11 days	
3 Babcock	F	25	Death	Several days, death from pulmonary embolism	
4 Barr and Bulger	F	56	Improvement, death later	14 months	
5 Barr and Bulger	M	38	Improvement	2 months	
6 Beek	F	41	Death	20 days, necropsy revealed no remaining parathyroid tissue	
7 Beyerineck	F	35			
8 Boyd, Milgram and Stearns	M	21	Improvement	3 months	
9 Chievitz and Olsen	F	25	Improvement	10 months	
10 Churchill and Cope	F	46	Relief	25 months	
11 Churchill and Cope	F	60	Improvement	18 months	
12 Churchill and Cope	F	13	Improvement	13 months	
13 Churchill and Cope	F	41	Improvement		
14 Churchill and Cope	F	55	Improvement		
15 Churchill and Cope*	M	34	Improvement	6 weeks death from uremia and shock after removal of kidney stone	
16 Churchill and Cope	F	36	Improvement	6 months	
17 Churchill and Cope	F	44	Improvement		
18 Churchill and Cope	M	35	Improvement	3 months	
19 Churchill and Cope	F	54	Improvement		
20 Churchill and Cope	F	33	Improvement	10 weeks	
21 Cohen and Kelley	F	45	Improvement	3 months	
22 Compere	F	50	Improvement	4 years	
23 Cooley	F	14	Improvement	4 months	
24 Copello and Barlaro	M	34	Improvement		
25 Cosin	M	17	Improvement	5½ months	
26 Eggers	F	39	Improvement	7 months, death from accident	
27 Elmslie, Fraser, Dunhill, Vick, Harris and Dauphinee	F	42	Improvement	2 years	
28 Elmslie et al	F	26	Improvement	20 months	
29 Elmslie et al	F	23	Improvement	16 months	
30 Frugoni and Alessandri	F	18	Improvement	4 months	
31 Gold	F	54	Improvement	3 years	
32 Gordon Taylor, Wiles and Baker	F	20	Improvement		
33 von Hecker			Improvement		
34 "	F	42	Improvement	13 months	
35 "	F	44	Improvement	9 months	
36 "	F	41	Improvement	17 months	2 adenomas
37 Hunter	F	37	Improvement	10 months,	2 adenomas
38 Hunter	F	49	Improvement	10 months	
39 Hunter	F	51	Improvement	5 months	
40 Ianz	M	56	Improvement		
41 Leri, Layan, Lièvre and Weil	M	31	Improvement	16 months	
42 Mandl	M	38	Improvement	3½ years	
43 May and Lièvre	M	45	Improvement	3 months	
44 Pemberton and Geddie	F	14	Improvement	1 month	
45 Quick and Hunsberger	M	25	Improvement	1 month	
46 "	F	50	Death	4 days	
47 "	F	24	Improvement	1 year	
48 "	M	36	Improvement		
49 Schlesinger and Gold	F	42	Improvement		
50 Schmitt	F	51			
51 "	M	56	Improvement	2 years	
52 "	F	35	Improvement	10 months	
53 Struthers	F	38	Death	Accident a few days	
54 Toland	F	60	Death	4 months	
55 Toland	F	42	Relief		
56 Venables	F	52	Improvement		
57 Wanke	F	41	Death	19 days, large adenoma and a second gland, the size of a coffee bean removed	
58 Weil, Langlois and Dragomirescu	F	44	Improvement	3 weeks	
59 Wehmann	F	45	Improvement		
60 Wilder	F	32	Improvement	3 months	
61 Wilder, Camp, Robertson and Adams	F	48	Improvement, death later	18 months	
				10 weeks, pain diminished but tetany and later nausea and vomiting developed	

the diagnosis of parathyroidism if all other symptoms speak for it." The most definite and pathognomonic finding in cases of true hyperparathyroidism due to adenomatous tumor is that of a negative calcium balance, but Bauer and his associates have found that in every case of ankylosing polyarthritis in their series the calcium balance was positive. No reports have been published by the authors who advocated parathyroidectomy in cases of ankylosing polyarthritis to show the results of their studies on the metabolism of calcium and phosphorus.

Leiche and Jung reported slight elevation of the calcium content of the serum in only 3 of 20 cases of ankylosing polyarthritis which they studied. Parathyroidectomy was attempted in each case. Marked

TABLE 12—*Summary of Cases of Nephrolithiasis and Hyperplasia of the Parathyroid Glands Without Decalcification of the Skeleton*

Author	Sex	Age, Years	Calcium, Mg per 100 Cc	Phosphates, Mg per 100 Cc	Comment
Albright, Aub and Bauer (case 12)	F	51	11.5	3.1	Renal calculus, coxalgia, no osteoporosis, no adenoma noted
Albright, Aub and Bauer (case 13)	M	22	15.8	2.8	Renal calculus on right side, no osteoporosis, removal of 1 large hyperplastic parathyroid gland, improvement reported
Albright, Aub and Bauer (case 15)	F	62	15.0	2.2	No decalcification, bilateral kidney stones, 2 large parathyroid glands (hyperplastic) and part of a third removed, no subsequent report
Albright, Aub and Bauer	M	26	16.7	1.7	No skeletal changes, 2 stones in right ureter, 2 hyperplastic parathyroid glands removed, no subsequent report
Albright, Aub and Bauer (case 17)	F	55	12.4	2.1	Ureteral stone, no changes in the bones, 3 large glands and a portion of a fourth removed, no tetany, hyperplasia, no subsequent report

symptomatic improvement was reported in the first case, but six months after the operation the patient suffered a relapse and was worse than at the time of the first admission. The authors at this time tried the intramuscular injection of parathyroid extract in this patient and again reported improvement. In the second and third cases there was also improvement, but the pathologist was not able to discover parathyroid tissue in the specimen removed in the second case. Apparently, the improvement in this case was just as marked as in those in which the parathyroid tissue was definitely excised.

In a number of cases studied by Ssamarn in which operation was performed by Oppel, no parathyroid tissue was noted in the specimen removed. That the patients showed improvement comparable to that of the patient whose glands were removed indicates that another factor must have accounted for this change. Welti and Bauer agreed with

glands in a child is surprising and it suggests that tumor of the parathyroids was present but was not noted by the surgeon. The relapse in the case of Hannon, Shorr, McClellan and DuBois and the subsequent observation by Churchill and Cope of a mediastinal tumor in the same patient causes one to doubt whether the recovery reported in the other cases in which only normal glands were excised will be lasting.

TABLE 3—*Thirty Cases in Which an Adenoma of the Parathyroids Was Removed at Operation But Clinical Data Were Not Reported*

	Author	Sex	Age, yrs	Comment
1	Balla			Twenty two cases of generalized osteitis fibrosa, detailed reports lacking
2	von Disque			Improvement reported adenoma, probably same case as that of Rosenbach and von Disque
3	Dresser and Hampton	F	44	Adenoma removed
4	Hampton and Osman	M	14	Cited by Cosin
5	Hampton and Osman	F	43	Cited by Cosin
6	Redwitz			Too recent for report, adenoma the size of a cherry stone
7	Schnabel	M	26	Improvement probably same case as that published by Quick and Hunsberger
8	Schaldemose			Improvement 2 adenomas, cited by Chervitz and Olsen
9	Shallow (case 1)	F	29	Improvement

TABLE 4—*Eight Cases of Hyperparathyroidism in Which No Tumor Was Observed at Operation But One or More Parathyroid Glands Were Removed*

	Author	Sex	Age, yrs	Comment
1	Barrenseheer and Gold	M	13	No improvement 1 year after operation
*2	Baur, Albright and Aub			Same case as that reported by Hannon Shorr et al. Richardson, Aub and Bauer, and others 2 normal glands removed
3	Cooley	F	17½	Improvement
4	Dresser and Hampton	F	41	Later irradiation of glands no improvement
*5	Hannon Shorr McClellan and Du Bois	M	30	Improvement 2 years after operation
6	Hitzrot and Comroe	F	42	Improvement 5 months later
7	Landon	M	2½	Improvement, 3 normal glands removed
8	Shallow, case 2	M	12	
9	Wendel, case 2		17	No improvement

\* This is the case in which at the seventh operation Churchill and Cope (table 1) observed a large mediastinal adenoma of the parathyroids.

Supportive measures, including an increased mineral intake, may account for the improvement reported in several cases.

Nine cases are reported in table 5 in which no tumor of the parathyroids could be observed at operation. No parathyroid glands were removed. In the cases of Wendel, Terebinskiy and Dr. Phemister and me,<sup>1</sup> a tumor was excised, but it proved to be a nodule of the thyroid gland. No improvement was noted in any case.

1 Unpublished data.

me that the evidence is not sufficient to show that in any case of ankylosing arthritis there was also true hyperparathyroidism, although some symptoms of this condition may be found. Furthermore, it is significant that ankylosing polyarthritis was not described in any of the 124 reported cases of generalized osteitis fibrosa, in most of which the calcium content of the serum was high and the amount of inorganic phosphates low and in which an adenoma of the parathyroids was removed at operation or on postmortem examination. Bodansky, Blau and Jaffe and Johnson produced typical generalized osteitis fibrosa in experimental animals by injecting parathyroid extract, but in none of these animals did arthritis develop. There is evidence that ankylosing polyarthritis may be a deficiency disease, similar to rickets or osteomalacia. The typical micro-pathologic picture of the enlarged parathyroid glands in all three conditions is that of simple hyperplasia and may represent a compensatory change (fig 2A). The success of Fletcher in treating multiple arthritis by means of diets rich in vitamin and mineral content lends support to this theory.

#### OSTEITIS DEFORMANS (PAGET'S DISEASE)

In Paget's disease the calcium metabolism, as demonstrated in the present series and also by Hunter, Rabinowitch, Van Hazel and Andrews, and DeCosta, Funk, Bergeim and Hawk, usually shows a marked positive balance with a greatly diminished excretion of calcium by the kidneys.

A review of 9 cases of Paget's disease studied in the University of Chicago Clinics during the past five years is presented. The ages of the patients ranged from 53 to 67, which confirms the impression that osteitis deformans is a disease of late adult life. In each case there was pain in the lower part of the back or in the lower extremities. The calvarium was involved in only 4 cases. Various types of therapy were used, but it is difficult to estimate the value of any of them. The average calcium content of the blood serum was slightly lower than normal, and the phosphorus content of the blood slightly higher, before medication was begun. There was a slight increase in the calcium content of the blood and a decrease in the phosphorus content after therapy with viosterol or parathyroid extract was instituted.

Erdheim observed no tumor of the parathyroid glands at autopsy in patients with Paget's disease. Gold reported the pathologic studies of Maresch, who made postmortem examinations of the parathyroid glands in 40 cases of Paget's disease, and those of Schmol, who completed 170 necropsy studies of Paget's disease. No tumor of the parathyroids was noted in the entire series. Excision of parathyroid glands in cases of osteitis deformans may be an error, as thyroidectomy would be in instances of myxedema.

of normal dogs with 2,000 roentgen units without effect on the amount of calcium or inorganic phosphates in the serum. I carried out independently a similar experiment, the parathyroid glands being irradiated

TABLE 7—Cases in Which the Clinical Diagnosis Was Parathyroid Osteosis and Roentgen Therapy Was Given to the Parathyroid Region

Author	Sex	Age, Yrs	Comment
1 Biedl	F	19	Improvement
2 Chabe	F	33	'Helium' therapy
3 Compere and Phemister	F	56	Irradiation after failure to find parathyroid adenoma at operation; improvement doubtful after 3 months (table 5)
4 Dresser	F	41	Irradiation after removal of 2 normal glands; no improvement (table 4)
5 Dresser	F	35	Irradiation, no improvement (table 5)
6 Gutman, Swenson and Parsons	F	60	Irradiation in a far advanced stage, but the patient died; 2 adenomas noted at necropsy (table 8)
7 Hellstrom	M	54	Irradiation only, improvement; cyst of mandible healed
8 Merritt	F	74	Improvement; patient "cured"
9 Weil, Aime and Langlois (case 1)	F	46	Improvement; later death from uremia; no report of autopsy

TABLE 8—Cases in Which Parathyroid Adenomas Were Observed at Postmortem Examination

Author	Sex	Age, Yrs	Comment
1 Ask Upmark	M	46	Adenoma size of hazelnut; deposits of calcium in kidney
2 Berner	F	40	Adenoma, renal calculus
3 Berner	F	47	Adenoma, renal calculus
4 Dawson and Struthers	M	49	Parathyroid tumor
5 Hadfield and Rogers	F	38	Soft, yellow, cystic tumor, no skeletal changes
6 Hadfield and Rogers	M	51	Palsading of cells, no remission but definite tumor, clinical diagnosis, acromegaly
7 Giordano (case 1)	F	26	Adenoma
8 Gutman, Swenson and Parsons	F	60	Irradiation of 2 cystic adenomas (table 7)
9 Hanke (case 1)	F	33	Two adenomas; deposits of calcium in kidneys; blood calcium, 16.9 mg
10 Hanke (case 2)	F	49	Two adenomas; deposits of calcium in kidneys; blood calcium, 23.4 mg
11 Lambie	F	30	Parathyroid adenoma, serum calcium 17 mg, phosphorus, 2.7 mg
12 Lebl	M	42	Two adenomas
13 Noble	M	40	Parathyroid adenoma, a few small calcified masses in kidneys; serum calcium, 13 mg; previous unsuccessful exploratory operation for tumor
14 Pereira and Freire			Parathyroid tumor
15 Renaud, Petit Maire and Fayot			Retrosternal adenoma of parathyroid
16 Salnton and Milot (case 1)	F	50	Adenoma
17 Schupp	F	51	Parathyroid adenoma
18 S—			Adenoma size of hazelnut
19	M	47	Adenoma of parathyroid
20	F	48	Small adenoma
21 W—	F	41	Adenoma

directly after exposing them and the other structures of the neck being protected by a sterile lead shield. No changes in the blood chemistry were observed and there were no demonstrable changes in the bony skeleton of the dogs during the six months following the irradiation.



The high calcium content of the serum and the low percentage of inorganic phosphates in the plasma in cases of generalized osteitis fibrosa (parathyroid osteosis) are in sharp contrast to the usual normal values in cases of Paget's disease. This contrast is best shown in 7 cases of parathyroid osteosis reported by Comper, Hunter, and Boyd, Milgram and Stearns. In these cases the calcium content of the serum ranged from 12 to 21 mg per hundred cubic centimeters of blood, and the average amount was more than 6 mg higher than that found in each of 7 cases of Paget's disease and 7 cases of localized osteitis fibrosa studied in the University of Chicago Clinics. In the last two conditions

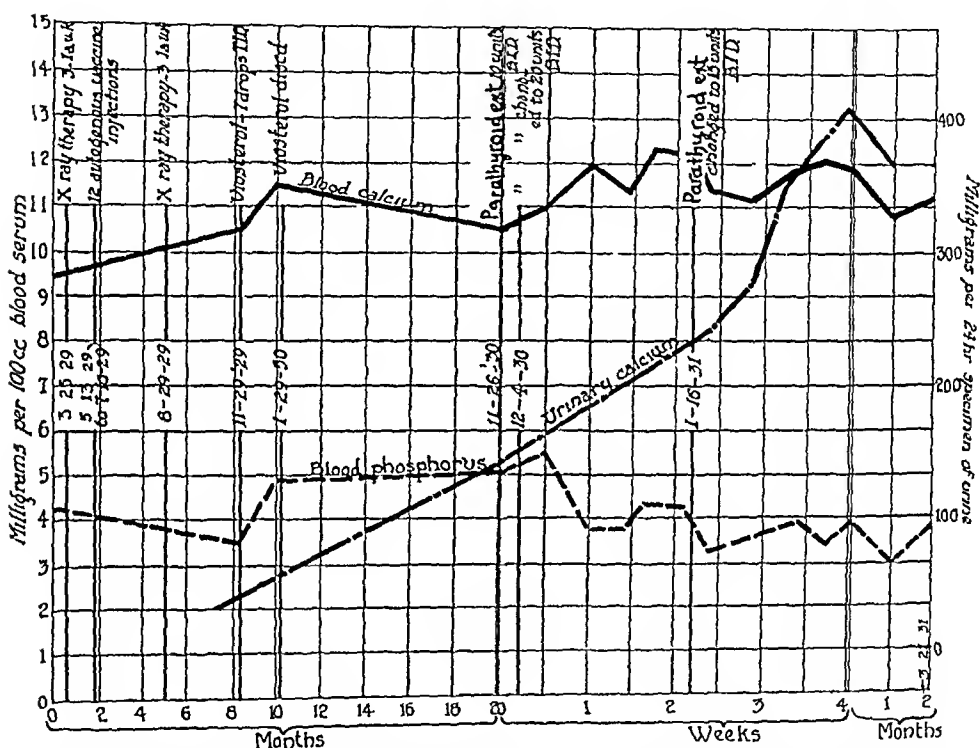


Fig 3—Changes in the calcium and inorganic phosphate contents of the blood and the excretion of calcium in the urine in a case of Paget's disease observed for a period of two years

all the determinations of the calcium content of the blood were within the lower limits for normal values. In cases of generalized osteitis fibrosa the amount of inorganic phosphates in the serum ranged from 1.2 to 3.2 mg per hundred cubic centimeters, while in cases of Paget's disease and of localized osteitis fibrosa the values varied from 3.5 to 5.5 mg. The higher values were found in cases of children. The following history of 1 of the cases of osteitis deformans in this series is characteristic:

L. B., a man aged 57, came to the University of Chicago Clinics in March 1929, complaining of pain in the lumbar region and bowing of the thighs of twenty

and Erdheim and in studies of experimentally produced rickets by Pappenheimer and Minor Doyle, Nomidez and Goodale, Higgins, Foster and Sheard, Erdheim, and Luce. In some cases the parathyroid glands became ten times the normal size, and the microscopic sections revealed benign hyperplasia similar to that described by Ballin and Moise in enlarged glands removed from patients suffering from ankylosing polyarthritis. Treatment of rickets with diet and vitamin D resulted in a decrease in the size of the tumors. Since these tumors were produced on a deficient diet and receded when the deficiency was corrected the hyperplasia in this condition may be described as compensatory.

TABLE 11—*Recapitulation of Data in 75 Cases of Parathyroid Osteosis Reported in Tables 1 and 10\**

A Clinical Data		No of Cases
Sex of Patient		
Female		56
Male		17
Not stated		2
Tumor palpable in neck before operation		16
Renal calculi		20
Mottling of calvarium as described by Camp		29
Bone cysts		46
Giant cell tumors of bones		24
Pathologic fractures		41
Improvement reported		61
Evidence of recalcification of bones after operation		25
Tetany after operation		37
Death after operation		7
Death occurring later after temporary improvement		4
Death as a result of metastases from primary carcinoma of the parathyroid glands		1
B Data on Blood Chemistry		
Calcium content of serum before operation, mg per hundred cubic centimeters		
Maximum, 21 (Beyerinck)	21.6 (Lanz)	19.8-38 (Leri)
Minimum, 9-12.5 (Babcock)		
Average (approximate), 14		
Amount of inorganic phosphates before operation, mg per hundred cubic centimeters		
Maximum, 3.3 (Gutman, Swenson and Parsons)		
Minimum, 1.2 (Barr, Bulger and Dixon)		
Average (approximate), 2.2		

\* The ages in these cases ranged from 65 to 13 years. London reported the case of an infant aged 2½ years, but no tumor was seen at operation (table 4).

#### MULTIPLE ANKYLOSING ARTHRITIS

Oppel, Ssamain, Leniche and Jung, Ballin, Funsten, and Simon have reported clinical improvement in cases of ankylosing polyarthritis after parathyroidectomy. A review of the microscopic studies as well as of the photomicrographs has failed to demonstrate true adenoma of one or more parathyroid glands in these series. Enlargement of the glands in some cases was reported, but the cellular picture was that of simple hyperplasia. The authors who reported these studies accepted the clinical syndrome of generalized demineralization of the bones, hypotonia of the muscles, lengthening of the chonaxia and increase in the calcium content of the serum as sufficient evidence for a diagnosis of "parathyroidism." Ballin and Morse also stated that "hypercalcaemia can be temporarily or continuously absent and if so should not exclude

the amount of calcium in the blood increased slightly, and the level of the phosphorus content fell, but all the values were within the normal range. The striking feature was the amount of calcium in the urine. This was only 30 mg for each period of twenty-four hours before treatment. The average normal excretion of calcium is about 180 mg for twenty-four hours, as reported by Bauer, Albright and Aub for a large series of cases. This value suggests the positive calcium balance so often found in the cases of Paget's disease reported by DaCosta, Van Hazel and Andrews and Rabinowitch, and it is in sharp contrast to the markedly

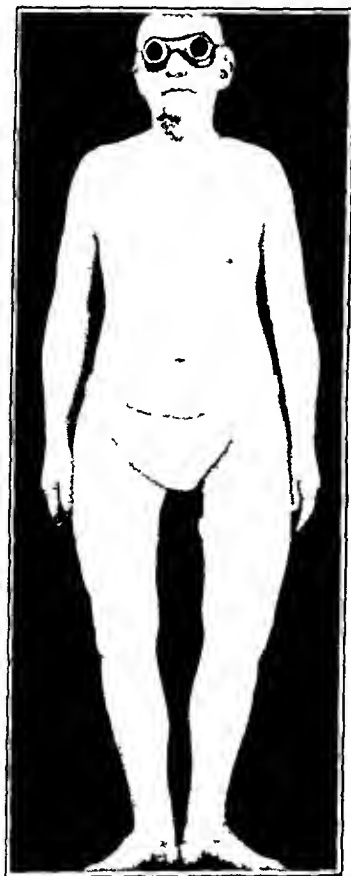


Fig 5—Photograph of a patient (L. B.) with Paget's disease, showing the bowing of the femurs and the external rotation of both legs

increased calcinuria found in cases of parathyroid osteosis. The excretion of calcium in the urine increased to 140 mg after two months of treatment with viosterol and then rose to 430 mg for periods of twenty-four hours after four weeks of administration of parathyroid extract.

The value of this treatment is difficult to estimate, although symptomatic improvement was observed. Zimmer reported a case of osteitis deformans in which clinical and roentgenologic improvement occurred after treatment with parathyroid extract.

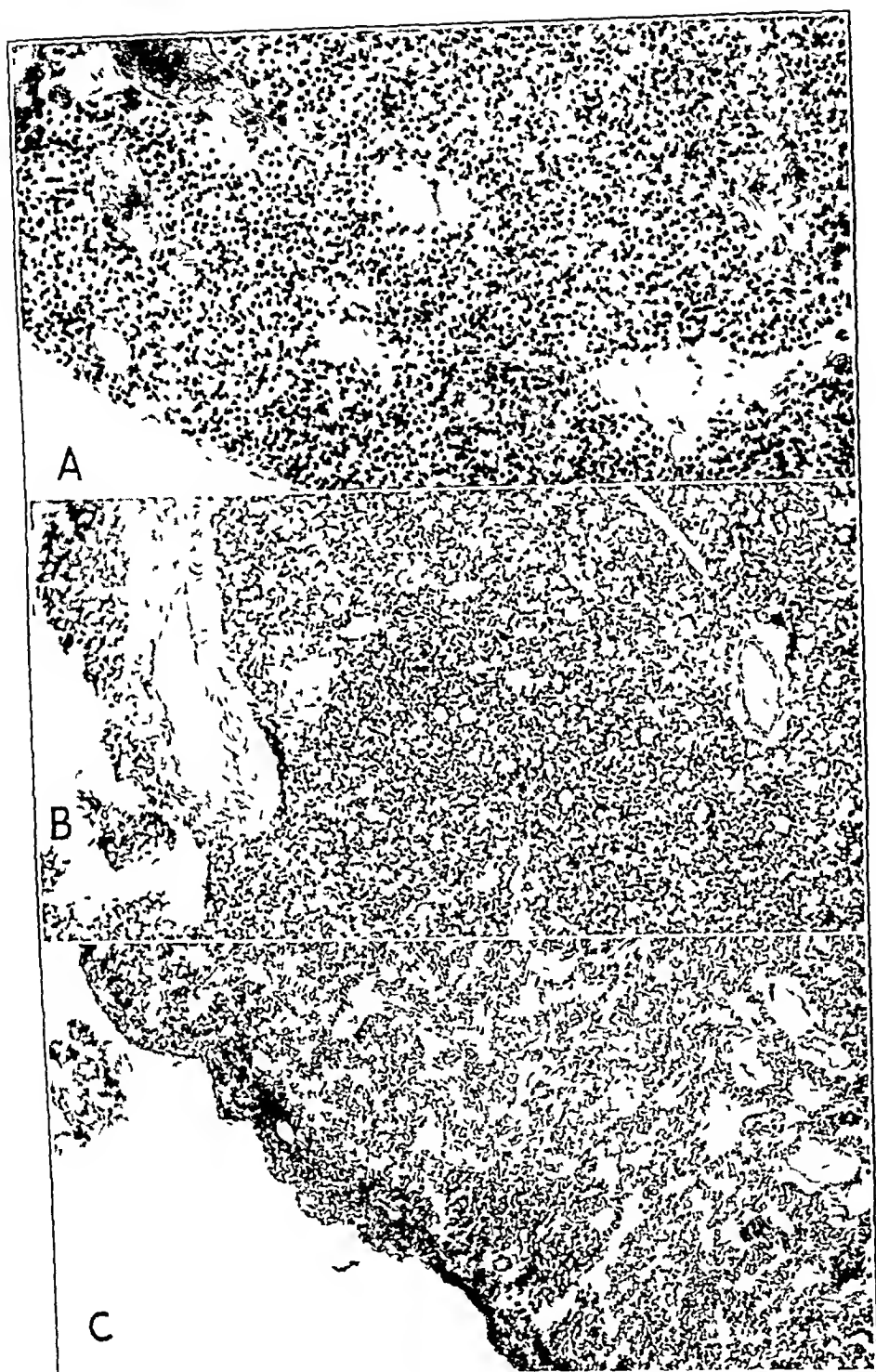


Fig 2—Photomicrographs of tissue from (A) a parathyroid gland in a case of Paget's disease of twenty years' duration, showing the normal cellular structure  $\times 130$  (B) an adenoma of the parathyroid gland, showing the compact cellular structure, trabeculae and absence of fat cells,  $\times 70$ , and (C) a normal parathyroid gland, showing the loose arrangement and the number of fat cells,  $\times 70$

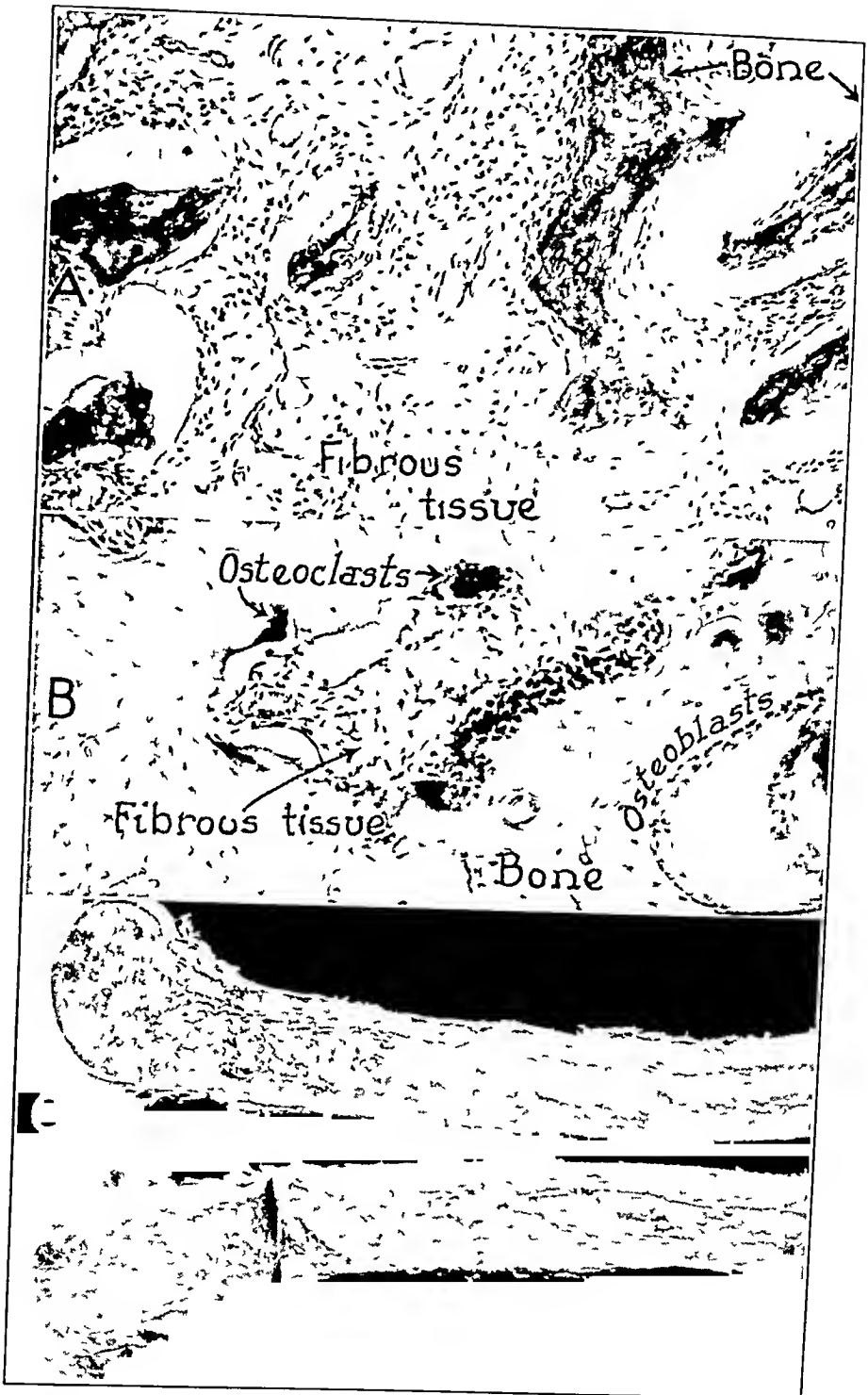


Fig 7—Photomicrographs of sections of bone in cases of (A) osteitis fibrosa with resorption and replacement of bone by fibrous tissue,  $\times 120$ , and (B) Paget's disease, in which the trabeculae of the bone are thick and the formation of bone is more marked than the absorption,  $\times 115$ . Photograph of a longitudinal section of long bone (C) in a case of Paget's disease, showing the thickened cortex and the narrow medullary canal.

131 13—*Review of 9 Cases of Paget's Disease Studied in the University of Chicago Clinics*

Blood Calcium and Phosphorus, Mg. per 100 Cc.											
	Date	Age	Sex	Symptoms and Duration	Bones Involved	Therapy	Before Medication		After Medication		Comment
							Calcium	Phosphorus	Calcium	Phosphorus	
W B	2/27/21	41	M	Pain in leg and bowing of tibia, 8 years	Skull, left femur and tibia	2 series of 3 roentgen irradiations	8.97	5.71	8.93	4.16	Mitral stenosis 5 years increase in local temperature left tibia 3.6 C warmer than right
C S	1/10/29	33	M	Pain in leg and lower part of back and bowing of tibia 20 years	Generalized	1 series of 3 roentgen irradiations	8.99	3.82	11.62	5.1	Weakness and nervousness 2 years basal metabolic rate, +12 increased local temperature, left tibia 2.5 C warmer than right
I B	1/1/20	57	M	Pain in lower part of back and legs, 20 years bowing of thighs, 13 years	Generalized	Röntgen irradiations 2 series of injections of autogenous vaccine, vitaminol for 2 months parathyroid extract, 9 months	9.51	1.26	12.20	3.75	Testis removed at age of 37 for tuberculosis (?)
O B	1/18/29	61	M	Pain in right thigh 10 years, limp, 6 months	Pelvis and femurs	Parathyroid extract, 15 units twice a day	10.54	1.02	11.80	3.60	Mild diabetes for years
G B	1/1/31	59	M	Pain and swelling in left leg 15 years, gradual increase	Left tibia		11.50	5.00			Decompression, osteotomy of left tibia, 12/21/32, some relief from pain
B B	10/7/29	55	F	Pain in lower part of back and left leg and bowing of left femur, 20 years	Left femur	Röntgen irradiation, 10 treatments for 10 months	10.65	4.70	11.50	6.10	Basal metabolic rate, -2
I H	2/2/31	59	M	Swelling of left fore arm, 13 years bowing of tibia, 2 years pain in right heel, 1 year	Pelvis and left femur, tibia and radius	Parathyroid extract, 15 units twice a day for 2 weeks	10.10	5.56	11.00	5.70	Basal metabolic rate, -9
I I	11/10/28	67	F	Pain and bowing of right thigh with limp, 10 years	Right femur	292 tablets 1/75 grain (78 mg.) of phosphorus, 1 series of 3 roentgen irradiations	9.10	5.10			Shortening of leg in 1928 about 1 1/4 inches, shortening in 1932, 2 1/4 inches
H C	6/7/32	59	M	Stiffness in legs, 7 years pain in thighs, 2 years	Skull, pelvis and femurs		10.90	2.40			

TABLE 14—*Factors Concerned in Differential Diagnosis of Conditions Characterized by Demineralization of the Bones*

Disease	Osteo porosis	Cysts 1 Giant 2	Patho logic Fractures	Condi tion of Muscles	Chronic Arthritis	Pain	Characteristic Changes	Serum			Amount of Calcium in Urine	Galeum Balance	Sulfur Reten tion	Parathyroid Glands	
								Calcium Content	Phos phorus Content	Phos phorus Content					
Parathyroid osteosis (gen eralized oste itis fibrosa cystica or Reck linghausen's disease)	General	1 Common 2 Common	Present, compression of vertebral bodies common	Hypo tonia	In spine or long bones of lower extremities	None	None	Normal or lower	Normal or higher	Decreased	Positive	Negative*	No definite or true adenoma re ported in an accepted case of Paget's disease	Adenoma Tumor of* one or two glands usually of normal size and micro scopic structure	
	Hypor ostosis enlarge ment and thickening of skull often present	1 Present 2 None	Less com mon	Hypo tonia	In long bones or spine	None	None	Normal or lower	Normal or higher	Decreased	Positive	Negative	No true adenoma	All para thyroid glands may show en largement with nor mal cell structure (probably compens atory)	
Ankylosing polyarthritis	General	1 None 2 None	Uncom mon compression of verte bral bodies common	Hypo tonia	In joints and spine	Calcifica tion of para vertebral ligaments with anky losis of the joints	Calcifica tion of para vertebral ligaments with anky losis of the joints	Occa sionally higher than normal	Normal	Normal	Positive	Positive	Positive balance	No true adenoma	All para thyroid glands may show en largement with nor mal cell structure (probably compens atory)
Osteomalacia	General	1 None 2 None	Occa sional bending of bones common	Hypo tonia, occ sional tetany	In long bones or spine	None	None	Low	Low	Normal or lower	Negative	Negative slightly estab lished	Observed in a few instances of osteo malacia associated with high calcium content of the serum	Frequent enlarge ment of all glands as reported at autopsy probably compens atory	Common (compens atory)
Rickets	General	1 Occa sional cystlike areas	Occa sional	Hypo tonia rare	Not com mon	None	None	Low or normal	Low	Low	Positive	Not con stant	Rare	Common (compens atory)	Common (compens atory)
Osteogenesis hyperphosphatemia	General	1 None 2 None	Very common	Hypo tonia	Not char acteristic	None	None	Normal	Normal	Normal	Positive	Not re ported	None	Reported in 1 case	Reported in 1 case
Osteitis fibrosa, localized and regional	Normal density of bone except in local or regional areas	1 Local solitary or regional	Common at site of lesion	Normal	At site of lesion only	None	None	Normal	Normal	Normal	Positive	Normal	None	None reported	None reported

\* These findings are of pathologic significance in the diagnosis of generalized osteoporosis.

years' duration. The symptoms had begun with mild pain in the lower part of the back and had progressed until he had difficulty in walking or bending forward.

Physical examination revealed an elderly white man, walking with a peculiar slow, shuffling gait with the thighs and feet rotated outward (fig 5). They could be rotated inward about 30 degrees with difficulty. There was marked bowing of both thighs.

Roentgenograms revealed marked anterior and lateral bowing of the femoral shaft and gross thickening and encroachment of the cortex on the medullary canal. Both trochanters had a cystic appearance, and the tuberosity of the ischium was involved. The lower dorsal and the lumbar vertebrae and the entire pelvis showed thickening, broadening and irregularly increased density (fig 6).

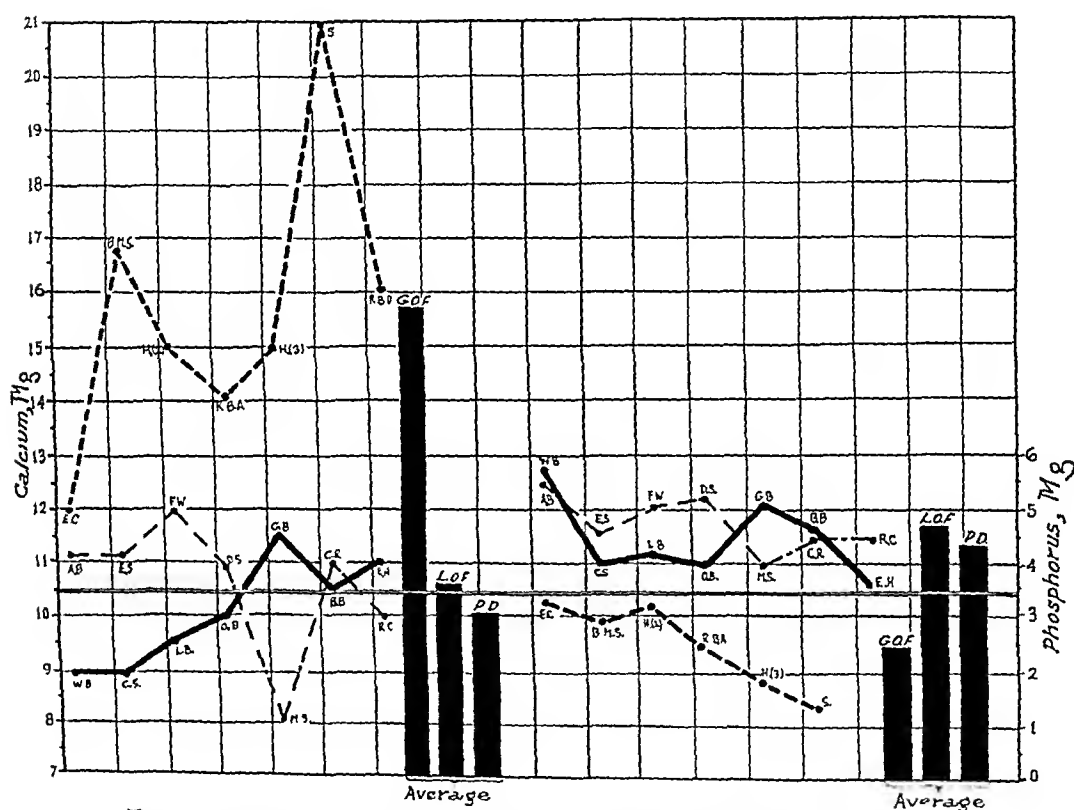


Fig 4—Curves for the calcium and phosphorus contents of the blood serum in cases of generalized osteitis fibrosa, localized osteitis fibrosa and Paget's disease. In this chart the values for cases of generalized osteitis fibrosa are shown by a line of dashes, those for localized osteitis fibrosa, by a line of dots and dashes, and those for Paget's disease, by a solid line. The calcium and phosphorus contents of the blood serum in cases of true hyperparathyroidism due to parathyroid adenoma and the values in cases of osteitis deformans are in contrast. The average value for the calcium content of the serum for 7 cases of generalized osteitis fibrosa (G O F) is almost twice that for 7 cases of localized osteitis fibrosa (L O F) or for 7 cases of Paget's disease (P D), while the ratio for the phosphorus content of the serum in the three conditions is reversed.

The patient was given roentgen therapy, autogenous vaccines, viosterol and parathyroid extract in succession. During observation for two and one-half years



## DYSCHONDROPLASIA

Dyschondroplasia, particularly of the rachitic type, has been classified with the "parathyroidism" presented in the group of cases reported by Ballin. Biochemically, there is no evidence to support this classification. Studies of calcium and phosphorus metabolism were made in this clinic on 3 patients, all of whom were found to show a positive balance. The results of two of these studies are shown in table 16.

"In normally growing children, there takes place during the ages between three and sixteen years an average daily storage of 0.01 Gm of calcium and 0.0008 Gms of phosphorus per kilogram of body weight per day" (Sherman, H. C., and Hawley, Studies on Twelve Children.)

TABLE 16—*Determination of Calcium and Phosphorus Balance in Cases of the Rachitic Type of Dyschondroplasia*

Experimental Period		Amount of Mineral In				Mineral Balance	
Number	Duration	Food, mM *	Feces, mM	Urine, mM	Total Out put, mM	mM	Gm per Day
H. M., aged 16 years							
Calcium							
I	3 days	144.22	104.82	17.71	122.53	21.69	+0.290
II	3 days	145.37	104.97	19.44	124.41	20.96	+0.280
Phosphorus							
I	3 days	154.56	81.36	63.11	144.47	9.89	+0.102
II	3 days	154.93	75.84	68.62	144.46	10.47	+0.105
F. G., aged 10 years							
Calcium							
I	6 days	224.21	201.05	3.35	204.40	19.81	+0.132
Phosphorus							
I	6 days	245.52	92.26	123.90	216.16	29.36	+0.152

\* mM indicates millimols

Heiter found that for the normal growth of the skeleton there must be an average daily storage of more than 0.1 Gm of calcium from the third to the sixteenth year.

Herbst studied the calcium metabolism for 6 normal boys between the ages of 6 and 14 years and found that from 0.01 to 0.016 Gm of calcium per kilogram of body weight was stored daily, or from 0.21 to 0.39 Gm per capita (Sherman). As indicated in table 16, in the cases studied in this clinic as much calcium was stored as would be needed for normal growth, according to the estimates of the basal requirement.

#### PATHOLOGIC LESIONS OF THE SKELETON IN PARATHYROID OSTEOSIS

A detailed description of the microscopic pathology of the bones has been given by Turnbull. The changes in the skeleton are lacunar resorption, fibrosis of the marrow and the formation of osteoclastomas and, in about 50 per cent of the cases of cysts. Lacunar resorption

A patient with marked Paget's disease of twenty years standing recently came to autopsy in this clinic and complete pathologic studies were made. The parathyroid glands were normal (fig 2A). Examination of the bones of the patient revealed involvement of both femurs and tibias (fig 7B). The long bones were bowed, and the thickness of the cortex was increased, ranging from 1 to 2 cm. The medullary canal was narrowed, and the bone marrow contained an unusual amount of fat and fibrous tissue. There was marked coxa vara of both hips due to loss of tensile strength.



Fig 6—Roentgenogram of the pelvic region of a patient (L B ) with Paget's disease. The trabeculae are wavy and distorted, the diameter of the shafts of the femur is increased, and numerous cystlike areas are evident.

The roentgenographic findings in the calvarium in a case of generalized osteitis fibrosa in a woman aged 59, showed definite small round areas of absorption in the dome of the calvarium resulting in a mottled appearance typical of this condition (fig 8B). When the skull in a case of Paget's disease is involved the roentgenograms show thickening of the bones of the dome with a resulting increase in the circumference of the skull. Many spherical areas of increased density may appear (fig 8C). In many instances of Paget's disease the skull is not involved while in roentgenograms in all the cases of hyperparathyroid-

by extensive, and in places complete, replacement of lamellar bone by trabeculae of fibrous bone. Apposition may be the predominant active process in a segment. The combination of resorption and apposition is shown by the action of osteoclasts and osteoblasts on different trabeculae in many sections, and even on the same trabecula in several sections. Trabeculae that are composed of several systems of fibrous bone further witness the interplay of the two processes. In focal areas the new spongy bone that has been formed may exceed or completely replace the normal spongiosa and compacta (fig 7A).

In osteitis deformans (Schnitz) the changes are similar with regard to lacunar resorption, but apposition and osteoblastic activity are more marked and regional areas of dense ossification or calcification are common (fig 7B).

#### TUMORS OF THE PARATHYROIDS

Diagnosis of adenoma of the parathyroid glands as an explanation of a condition considered to be due to hyperfunction of the tumorous glands may not be accepted without criticism. In discussing adenomatous changes in the thyroid gland Rienhoff declared that even though the cells lining the alveoli function locally there is no proof that these neoplasms produce a toxic secretion or evidence to suggest that the cells lining the alveoli function in such a manner as to influence the organism as a whole. Aschoff expressed the belief that adenomas of the parathyroid glands had nothing to do with the changes in the bone occasionally seen associated with them. Rienhoff also stated that adenoma and carcinoma of the parathyroid glands have in several instances been associated with a low calcium content of the blood and even with tetany.

Pathologically, the tumors in all the reported cases have been diagnosed as adenoma or as cyst of the parathyroid glands. Functionally such tumors resemble true hyperplasia. Both Ewing and Harbitz recognized the difficulty of differentiating moderate diffuse hyperplasia and true adenoma of the parathyroid glands. Tumors of the parathyroid glands grossly similar to those reported in this series and associated with similar skeletal conditions were studied by Eidheim and diagnosed as hyperplasia. Strauch studied a tumor removed from the neck of a woman who died after a typical attack of puerperal osteomalacia. His diagnosis of hyperplasia was based on the presence of all the normal cellular elements, while, according to his belief, only one type of cell is observed in true adenoma.

The tumor which was removed from a patient reported on from this clinic in 1930 was almost entirely composed of the one type of large epithelial cells with hyperchromatic nuclei and the predominating characteristic was formation of acini. No portion of the gland resembled the normal tissue of the parathyroids. One was justified then, from a pathologic standpoint in making a diagnosis of adenoma of the para-

ism which I have studied or reviewed the characteristic mottling of the calvarium has been noted

In table 14 I have attempted to compare several clinical syndromes which are characterized by local or general demineralization of the skeleton

As I have already stated, 'there is little evidence to indicate—and it would be difficult to rationalize the findings if it were so reported—that localized or regional bone lesions of the bone cyst and giant-cell



Fig 8—Roentgenograms of (A) a normal skull, (B) the calvarium in a case of parathyroid osteosis, showing mottling, and (C) the skull in a case of Paget's disease, showing thickening and enlargement of the calvarium and numerous areas of increased density

tumor type without any general skeletal involvement, could be explained on a metabolic basis." The secretions of the endocrine glands must be distributed to all parts of the body, and any marked effect which they may exert on the tissues should be manifested uniformly and not locally or regionally. Experience has demonstrated that these localized lesions heal after local excision and curettage or, in cases of giant cell tumor, with roentgen therapy, and this observation further discredits the theory

Metastases to the neck, mediastinum or pleura occurred in each case which he described

Beraud and Alamaidine reported 28 cases of epithelial tumor of the parathyroid glands, called by Fasiani malignant adenoma. Ferrero and Sacerdote reported a case in a woman, aged 65, with carcinoma of a parathyroid gland, metastases to the skeleton and pathologic fracture of the femur. Pepeire, Klemperer and Thompson reviewed cases of carcinomatous metastases to the parathyroid glands.

In the case of Guy the tumor of the neck had been noted for five years. When removed, the section showed a few acini and mitotic figures and areas of degeneration and cystic formation resembling those observed in the tumor in Wilder's case. A diagnosis of adenoma of the parathyroid glands was made, but the patient returned after eleven months with three new nodules near the operative scar. The author noted at this time that the general health of the patient was good and that there was no evidence of skeletal disease. These nodules and several glands in the posterior cervical triangle of the neck were removed, and all the specimens were observed to be carcinomatous. All the growths recurred in spite of roentgen therapy. Guy concluded from his studies that apparently benign tumors of the parathyroid glands of years' duration may suddenly take on malignant characteristics. While it is doubtful that the malignant changes in the tumor were responsible for the changes in the bone, which have been noted in so many other cases in which there was no suggestion of carcinoma, the cases reported in the literature of malignant tumor of the parathyroid glands help to substantiate the pathologic diagnosis of malignant growth in the cases of Wilder and Mandl.

Hoffheim, rejecting all cases in which the enlargement of the parathyroids was indefinite or inadequately described, collected from the literature 45 instances of measurable enlargement of one or more parathyroid glands. Of these, 27 were associated with definite disease of the bone including 17 instances of generalized osteitis fibrosa, 8 of osteomalacia and 2 of rickets. He cited increases to a size of 7 by 2.5 by 1 cm. The histologic changes were those characteristic either of hyperplasia or of adenoma, and it is important to note that sometimes more than one parathyroid gland was affected.

Bauer, Albright and Aub reviewed the reports of the cases in which examination at necropsy was made for lesions of the parathyroids. With their own cases and those of Maresch and Schmorl there were in all 327 cases in which definite disorder of the bones existed. These studies are analyzed in table 18.

Barr and Bulger listed 33 cases of tumor of the parathyroids in which coexisting changes of the bones were reported. These cases are included in the tables or the text of this paper.

of an endocrine etiology. The amount of calcium and inorganic phosphates in the serum in these conditions is found to be within normal limits.

Chronaxia has been described by Ballin as "an electric time coefficient of neuromuscular excitability defined as a minimal time in which current must pass through a muscle or nerve in order to elicit a reaction." This is not a specific test for hyperfunction of the parathyroids. Other conditions associated with weakness and general physical debility may give a similar delayed response. Mere fatigue in a normal person may alter the results of determinations of the chronaxia.

TABLE 15—*Localized and Regional Osteitis Fibrosa and Solitary Bone Cysts*

Patient	Date	Age, years	Sex	Calcium, Mg per 100 Cc	Phosphorus, Mg per 100 Cc	Comment
F W	2/14/31	8	F	12.20	5.10	Cyst of upper third of left humerus
M S	2/22/29	52	M	8.10	3.60	Cyst of upper end of left humerus and chronic arthritis
O R	12/15/30	56	F	11.08	4.44	Lesion of left 5th metacarpus
R C	10/26/31	12	M	9.99	4.40	Lesion of upper end of left humerus
D S	5/ 2/31	6	M	10.80	5.20	Lesion of upper end of right humerus
A B	11/24/30	20	F	11.15	5.75	Cysts of head of right femur
R M	8/ 3/32	16	M	11.00	6.10	Lesion of upper end of left humerus
B J	7/ 1/32	26	M	10.85	4.36	Pathologic fracture of upper end of right humerus
E S	11/21/30	21	M	11.20	4.44	Osteitis fibrosa localisata of neck of right femur
A C	6/ 6/30	10	M	12.10	4.00	Osteitis fibrosa localisata of left humerus and radius, no cavity
M K	4/ 6/31	32	F	11.50	3.70	Regional osteitis fibrosa of left femur and ilium

Too much emphasis has been laid on the elevation of the calcium content of the serum in certain of these conditions, and the equally significant determinations of the amount of inorganic phosphates in the serum or plasma have not been made. The only definite test for hyperfunction of the parathyroid glands which is acceptable is the study of calcium metabolism and the demonstration of a negative calcium balance. If patients with conditions representing the seven types of skeletal dystrophies listed in table 14 were studied while on a maintenance diet with the basal requirements of calcium and phosphorus and also of vitamin D, a positive balance would appear except in persons with parathyroid osteosis. In this condition the balance is consistently negative; the calcium content of the serum is high, the amount of phosphates in the plasma is low, and true adenomas of one or two parathyroid glands are noted in nearly all cases at operation or on postmortem examination.

estimation of the calcium content of the serum and the amount of inorganic phosphates in the blood, may not be of significant diagnostic aid in early cases of parathyroid osteosis. Determination of the amount of calcium in the urine for periods of twenty-four hours may help in confirming this diagnosis, while the more specific study of the amount of calcium lost by determination of the calcium and phosphorus balance for from three to six days is costly and difficult to make.

Chievitz and Olsen suggested functional tests for calcium. They found that an increase in the amount of calcium ingested in a case of parathyroid osteosis did not produce an increase in the excretion of calcium in the urine, but that there was a distinct increase after the intravenous injection of calcium chloride. In control tests on normal persons with either the ingestion or the intravenous injection of calcium, there was a consistent increase in the amount of calcium excreted in the urine. These tests indicate a defective absorption of calcium from the intestines in parathyroid osteosis and a decreased capacity of the organism for the retention of calcium.

Immediately after the removal of the parathyroid adenoma the tests were repeated. The output of calcium in the urine was constantly subnormal after ingestion and intravenous injection of calcium, indicating that the organism was now capable of depositing calcium.

A second diagnostic method has been reported by Hamilton and Schwartz of the department of pediatrics of the University of Chicago. These observers found that a large dose of calcium chloride or calcium gluconate, given by mouth, causes a much more marked increase in the calcium content of the serum of rachitic rabbits than in that of normal rabbits. This marked affinity for calcium in the blood of rabbits with rickets was thought to be due to hyperactivity of the parathyroid glands. Further evidence was offered to support this theory, and a test for the parathyroid hormone described by these authors was applied to the blood of normal and rachitic rabbits, which indicated an increase of the hormone in the blood of the rachitic animals. No blood from a patient with parathyroid osteosis was available for similar tests. This opens a field for future investigation, and the test may prove to be a simple and valuable aid in the early diagnosis of hyperparathyroidism.

#### TREATMENT OF PARATHYROID OSTEOSIS

Since the etiology of this disease is thought to be an excess of the secretion of the parathyroids due to enlargement and adenoma of one or more parathyroid glands, treatment consists first of removal or destruction of the tumors. The methods of surgical treatment have been individually and effectively described by Walton, Ballin and Churchill and Cope. Since death from tetany has been reported in 4 cases, it is essential that at least 2 normal parathyroid glands should

is predominant. Roentgenograms and histologic examination of the skeleton at necropsy show that resorption has led to general osteoporosis, which, however, varies in degree in different places (figs 7 A, 8 B and 9). But formation of bone does not cease. Bone is seen in the process

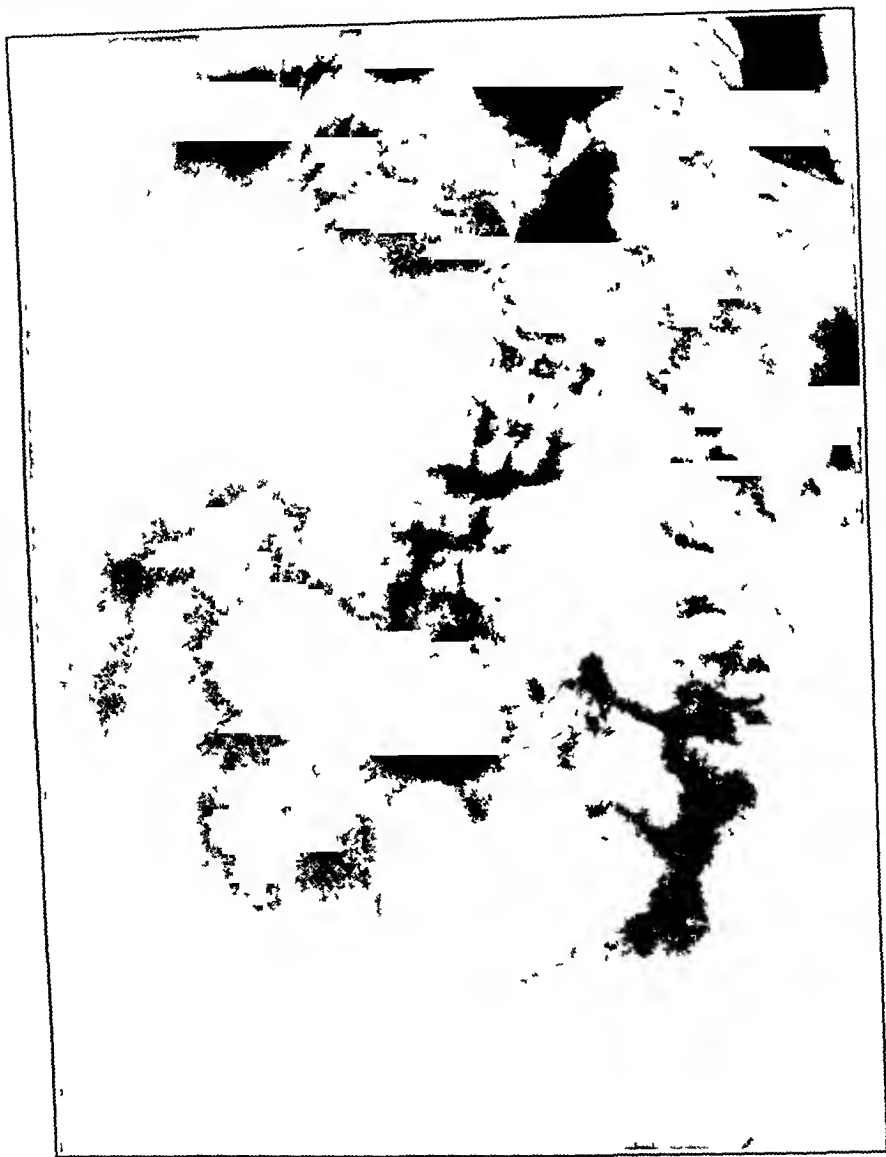


Fig 9—Roentgenogram of the pelvic region of a patient with parathyroid osteosis. The generalized demineralization of the skeleton in this case is in sharp contrast to that in the case of osteitis deformans shown in figure 6. Symptoms in this case became more marked during pregnancy, which at the time the roentgenogram was taken was approaching term.

of formation in almost all the sections taken from the more severely involved parts of the skeleton, and previous formation of bone is shown



phase of the disease is markedly positive, the output of calcium in the urine is decreased, and the parathyroid glands are usually observed to be of normal size and microscopic structure

Ankylosing polyarthritis is probably not caused by hyperparathyroidism, because in this condition, although the calcium content of the serum may be slightly higher than normal, the amount of the inorganic phosphates in the plasma is normal, the calcium balance is positive, and while the parathyroid glands are, according to reports, sometimes enlarged the enlargement is usually symmetrical, involving all the glands, and is similar to that reported in cases of rickets or of osteomalacia associated with a low serum calcium content. In animals with rickets the addition of vitamin D and of adequate amounts of calcium and phosphorus to the diet results in decrease in size of the enlarged parathyroid glands as well as in healing of the skeletal disease

Parathyroidectomy in cases of ankylosing polyarthritis or of Paget's disease is not justifiable unless there is more evidence of pathologic change or dysfunction of the parathyroid glands than has been described in reports of cases in the literature

Demineralization of the skeleton in cases of polyarthritis may be accounted for as atrophy of disuse

While removal of tumors of the parathyroid glands has not resulted in complete recovery in the reported cases, the symptomatic improvement, the chemical evidence of increased retention of calcium, and the roentgenographic evidence of increased density of the bones in the cases in which observation has been made for a sufficient period after operation are results which, as the operative risk is slight, warrant surgical intervention in cases such as those reported in this paper. Earlier diagnosis may lead to more favorable results, especially in the prevention of renal damage

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thyroids (fig 2 B) If this was compensatory hyperplasia it is difficult to explain why another gland removed from the same side was entirely normal (fig 2 C) If, then, the changes in the calcium metabolism in this and similar cases are assumed to be due to increased activity of the parathyroids, one must conclude that the adenoma produced an abnormal amount of parathyroid secretion, that there was hyperfunction of the grossly normal-appearing parathyroid glands or that there was in each case undiscovered and abnormally active accessory parathyroid tissue The presence of a pathologically similar tumor in a series of 124 reported cases lends weight to the first hypothesis

The tumors in the cases of Wilder, Mandl and Toland were classified as malignant adenoma because of the presence of mitotic figures, polymorphism of the cells, hyperchromatic nuclei and invasion of the neoplastic tissue into the capsule in Wilder's case and into the adjacent

TABLE 17—Summary of Micropathologic Features of the Parathyroid Glands

Characteristics of the Normal Gland or Benign Hyperplasia of the Parathyroids in Cases of Rickets, Osteomalacia, Metastatic Osteoplastic Carcinoma and Ankylosing Polyarthritis	Characteristics of Adenoma of the Parathyroid Gland Reported in 124 Cases of Generalized Osteitis Fibrosa Cystica (Recklinghausen's Disease)
Cellular elements diffuse or compact Definite arrangement of irregular strands or trabeculae Occasional acini Many fat cells Many foam cells Few granules in nuclei	Cellular elements very compact Less connective tissue and no strandlike arrangement of cells Numerous acini Few or no fat cells No foam cells Large, dark staining granules in nuclei of cells

muscles in Toland's case The striking absence of foam cells and fat, which Wellbloom mentioned, may not be a criterion of malignancy, for the same thing was true in my case and in other cases in which the results of pathologic study were reported in detail and in which there was no suggestion of malignant growth

The duration of disease of the bone in the cases of Wilder, Mandl and Toland for from five to eight years and the failure of recurrence for years after operation speak against a diagnosis of malignant tumor However, a review of the literature on malignant tumors of the thyroid and parathyroid glands indicates that in almost every instance tumor of some kind preceded the malignant changes for several years Balfour in a series of 63 cases of malignant struma, noted that in not a single case had the condition appeared suddenly but some form of diffuse or nodular goiter had preceded it Wilson found that in 157 of 290 cases of malignant goiter there had been enlargement for five years or longer In most of the 8 cases of malignant tumor of the parathyroid glands reviewed by Kocher, the tumor had been present for many years

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Hadfield and Rogers described 2 parathyroid tumors without parathyroid osteosis, 1 being associated with acromegaly. They included reports from the literature of 6 additional cases of adenoma of the parathyroids observed at postmortem examination of patients with acromegaly.

Enlargement of the parathyroid glands in a case of multiple myeloma was reported by Bai and Bulgei (case 3, 1930) and by Hunter in a case of generalized carcinomatosis.

Congenital dysplasia of the bones (osteogenesis imperfecta) associated with lesions of the parathyroids was described by Wyatt and McEachern, but the calcium and the phosphorus content of the blood were normal.

Adenoma of the parathyroids was noted by Claude and Schmeigeld in a patient with epilepsy without skeletal deformities or other evidence of hyperparathyroidism.

TABLE 18—*Analysis of 327 Cases of Definite Disorders of Bone*

Disorder of the Bones	Author Reporting Cases	Total Number of Cases	Condition of Parathyroid Glands
Rickets	Hartwick Schmorl Ritter	20	Hypertrophy in 2 cases
Senile osteoporosis or osteomalacia	Schmorl Strada, Maresch	40	Parathyroid glands normal
Osteitis deformans*	Maresch, Schmorl	210	All the parathyroid glands normal
Osteomalacia	Danisch, Strada Thomas von Verbely Bauer Hohlbaum	57	Hypertrophy in 27 cases adenoma in 1 case

\* Gold reported the results of postmortem examination in 40 cases of osteitis deformans in which Maresch found all the parathyroid glands normal. Maresch noted a large cystic tumor of the parathyroids in 1 case in which there was no demonstrable disorder of the bones. Schmorl observed no adenoma of the parathyroids in 170 postmortem examinations in cases of osteitis deformans.

#### NEED FOR EARLY DIAGNOSIS OF PARATHYROID OSTEOSIS

Diagnosis of parathyroid osteosis has usually not been made until the disease has progressed to the stage of marked decalcification with varying degrees of deformity and renal damage. The arrest of the progress of the disease, when so much pathologic change in both the bony framework of the body and the internal organs is present, cannot be expected to restore normal function. After six unsuccessful operations by various surgeons, Churchill discovered and removed a mediastinal tumor of the parathyroid glands from a patient who had been suffering from parathyroid osteosis for more than ten years. There was temporary symptomatic improvement, but the patient died of renal insufficiency and shock after an operation for the relief of ureteral obstruction from calculus, six weeks after the removal of the tumor.

Early diagnosis and prompt removal of the parathyroid adenoma would be expected to arrest the disease before severe renal damage had occurred. The chemical analyses, done as a routine including the

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be identified and left undisturbed. In the case described by Beck no parathyroid glands could be seen at necropsy after death from tetany twenty days after the excision of a tumor of the parathyroids and of one normal parathyroid gland.

Roentgen irradiation of the parathyroid glands resulted in improvement in 4 of 10 cases. Experimental evidence (Biedl and Compere) indicates that the function of the normal parathyroid glands is not disturbed by such irradiation, and the inference is that this procedure may be a safe method of ablation of the parathyroid adenoma. A much larger series of patients must be subjected to this treatment before definite conclusions can be made.

After ablation of the parathyroid tumor tetany has been prevented or controlled in most instances by ingestion or intravenous injection of calcium, injection of parathyroid extract or a combination of these measures.

Ingestion of calcium should be continued for a year or longer. Since the growing skeleton needs from 0.2 to 0.3 Gm. of calcium daily for its development, the markedly decalcified adult skeleton, which may have lost as much as 50 per cent, or more than 1,000 Gm., of the calcium salts, cannot be expected to regain its normal density and strength in less than from one to three years, even after a definitely positive calcium balance has been reestablished. Foods rich in calcium, such as milk, nuts and fruits, should be included in the diet.

The eating of foods that are rich in their vitamin content, especially the juices of the citrus fruits in vitamin C and cod liver oil or viosterol in vitamin D, is advised as an aid in the absorption or deposition of calcium salts. The importance of vitamin B may be questioned, but because of its recognized value in promoting better intestinal tone and function and in treating certain types of anemia, concentrates of yeast may be added to the diet.

#### SUMMARY

Parathyroid osteosis may be differentiated from other skeletal dystrophies which are clinically similar. This condition is characterized by weakness, pain in the long bones, generalized osteoporosis, deformities, a high calcium content of the serum, a low phosphate content of the plasma, an increased excretion of calcium in the urine and a negative calcium balance, an adenomatous tumor of one or more parathyroid glands has always been observed at postmortem examination and nearly always at operation, while the remaining glands are of normal size and structure. The results of study of 124 cases in which the diagnosis was verified at operation or autopsy are analyzed.

There is no good evidence that Paget's disease is caused by hyperparathyroidism. In this condition the calcium and inorganic phosphate contents of the blood are normal, the calcium balance in the chronic

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are consequently accused of malingering and, on the other hand, by the unnecessarily heroic measures that have been recommended and performed, for instance, amputation and, I believe, sympathectomy, as suggested from Leriche's clinic

Since Sudeck's description in 1900 acute bone atrophy has received considerable attention by German authors and, to a lesser extent, in the French literature. It was not, I believe, until 1926 that the phenomenon was specifically mentioned in the English literature. In January of that year Noble and Hauser<sup>5</sup> made an important contribution to the subject. After the publication of this article no specific reference to the lesion was made in the English literature until January 1933, when a very adequate consideration of the subject was made by Fontaine and Herrmann<sup>6</sup> from Leriche's clinic at Strasbourg. It is not surprising that this contribution, having its origin in Leriche's clinic, recommended sympathectomy almost to the exclusion of other methods of treatment. In connection with the appreciation of the physiology and pathology of bone, the English-speaking medical profession is, I believe, indebted to Moore and Key<sup>7</sup> for the translation into English of the valuable monograph published in 1926 by Leriche and Policard.<sup>8</sup> Key,<sup>9</sup> moreover, in 1933 contributed an article in which acute bone atrophy is accurately described, although individual cases are not analyzed.

Sudeck, in his original contributions, classified the disease into two stages, namely, the acute and the chronic form. It is the acute stage which is the more characteristic, more easily diagnosed, and, I believe, more susceptible to treatment.

#### DIAGNOSIS

The clinical diagnosis of acute bone atrophy can be presumed on the basis of typical signs and symptoms. Comparatively soon after an injury, which is usually trivial and is commonly in the neighborhood of the hand or foot, the extremity rather suddenly becomes swollen and extremely painful, particularly on movement. The skin loses its normal markings and becomes glazed in appearance, and discoloration of a dusky red appearance is seen. Although it is possible to palpate the

5 Noble, T., and Hauser, E. Acute Bone Atrophy, *Arch Surg* **12** 75 (Jan) 1926

6 Fontaine, Rene, and Herrmann, Louis G. Post-Traumatic Painful Osteoporosis, *Ann Surg* **97** 26 (Jan) 1933

7 Moore, Sherwood, and Key, J. Albert. The Normal and Pathological Physiology of Bone, St. Louis, C. V. Mosby Company, 1928

8 Leriche, Rene, and Policard, Albert. *La physiologie normale et pathologique de l'os*, Paris, Masson & Cie, 1926

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greater frequency in women, and among the nineteen cases twelve followed injuries of this nature

Acute bone atrophy as a posttraumatic phenomenon does not appear to occur in children, nor, as a matter of fact, have any cases been reported in aged persons

The nature of the injury antedating the development of posttraumatic acute bone atrophy is usually comparatively or actually trivial Colles' fracture or its variant occurred in twelve of the cases involving the hand, the injuries in the remaining seven cases were sprains or contusions Among the injuries of the shoulder, contusion alone is recorded as being responsible for five of the nine cases In one, fracture of the humerus had occurred, in one, fracture of the clavicle (fig 1), and in one dislocation of the shoulder joint with fracture of the great tuberosity

TABLE 1—*Tabulation of Cases of Bone Atrophy Reported in English Literature\**

	No of Cases	Age			Males	Fe Males	Part of Body Involved		
		Young est	Old est	Aver age			Shoul der	Hand	Foot
Noble and Hauser	47	19	64		21	26	1	5	41
Lontaine and Herrmann	22	25 (17)	65	37.7	14	8	6	8	8
Gurd	24	21	58	39.4	19	5	2	6	16
Total	93	19	65	38.6	54	39	9	19	65

\* Cases in which the spine was involved have not been included in this resume Otherwise the table represents, I believe, all cases reported in English literature susceptible of tabulation

Among the injuries of the lower extremity which anticipated the development of the osteoporotic phenomenon fractures of the ankle joint, usually grade 1, and fractures of one of the bones of the foot make up the greater number In one, a needle puncture wound of the tarsus, with no roentgenologic proof of injury to the bone, was the evident cause, and in several, sprains constituted the only history of injury One of my cases followed fracture of the tibia and one followed fracture of both bones of the leg, and in Noble and Hauser's series two cases are said to have followed fracture of both bones of the leg In twenty-seven of Noble and Hauser's cases the antecedent injury was specifically stated as being minor

An attempt has been made to analyze the cases reported and observed with a view to determining, if possible, what may be the cause or causes of the development of the lesion There appears to be no reason for suspecting a disturbance of the endocrine system, either of the pituitary or of the parathyroids since the phenomenon is essentially local There is apparently, also, no reason to believe that any

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development of the lesion becomes, therefore, one of determining, if possible, the reason why a sufficient grade of hyperemia is developed to bring about marked halisteresis. The matter is not yet settled, although it appears that the hyperemia responsible for the osteolysis is the result of nerve stimuli which are transmitted from the traumatized tissues through the spinal ganglions. Through reflex channels, therefore, a nimety of blood supply is induced.

Tables 2 and 3 indicate the relative incidence in different parts of the body, together with certain data with regard to the age spread and average age of those in whom the condition has developed.

TABLE 2—Data for Cases Involving the Hand

	No of Cases	Males	Females	Females			Males		
				Young est	Old est	Average	Young est	Old est	Average
Noble and Hauser	5	0	5	38	69	46.0			
Fontaine and Herrmann	8	3(2)*	5	41	65	56.8	47	57	52.5
Gurd	6	2	4	35	58	50.0	51	58	54.5
Total	19	5	14	75	69	49.9	47	58	53.2

\* Case 4—The patient, aged 17, presented no history of trauma. A diagnosis of tuberculous osteo arthritis was made from the roentgenographic picture. The condition, in my opinion, is not proved to be acute atrophy of the bones.

TABLE 3—Data for Cases Involving the Shoulder

	No of Cases	Males	Age		
			Youngest	Oldest	Average
Noble and Hauser	1	1			
Fontaine and Herrmann	6	6	30	57	47.5
Gurd	2	2	37	50	43.5
Total	9	9	50	57	46.5

One type of evidence appears to be usually, or invariably, present in the history of those cases which, in my experience, have progressed to the exhibition of acute bone atrophy following injury. As already stated, the original trauma is usually trivial. There is, however, almost invariably a history which suggests either prolonged or repeated insult to the traumatized tissues. The cases in this series (cases 15 and 19) of involvement of the hand and that of involvement of the carpus present substantially the same history. In one a severely comminuted Colles' fracture with marked displacement and in the other a comminuted fracture of the reversed Colles' or Smith's type was sustained approximately twenty-four hours before treatment of any sort was instituted. In both cases the patient was brought a considerable distance into town from the country by road without fixation and without protection to the injured limb.

# POSTTRAUMATIC ACUTE BONE ATROPHY

## A CLINICAL ENTITY

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In 1900 there appeared a publication by Sudeck entitled "Concerning Acute Inflammatory Bone Atrophy"<sup>1</sup> During the two following years the same author contributed two other articles under the titles, respectively, "Concerning Acute (Reflex) Bone Atrophy Following Inflammation and Injury to the Extremities and their Clinical Signs"<sup>2</sup> and "Concerning Acute (Trophoneurotic) Bone Atrophy Following Inflammation and Trauma of the Extremities"<sup>3</sup> Sudeck was particularly impressed by the patchy appearance of the bones in the type of osteoporosis which he described Of special interest in this regard is the fact that his first article dealt with what he considered to be an inflammatory lesion Although, in consequence of the ease with which the condition is demonstrated by means of roentgenographic examination, the osteoporotic lesion in the bone is most easily identified, it should, I believe, be borne in mind that the bony change is but one proof of acute atrophy of other structures Particularly, I believe, the atrophic changes in the ligaments and their attachments about the joints and in the cartilage covering the ends of the bones in the articulations deserve special attention in an effort to elucidate the problems of cause, prevention and cure of acute bone atrophy

In a former contribution<sup>4</sup> I expressed the opinion that the importance of acute bone atrophy as a cause of prolonged temporary disability is not sufficiently well recognized by the majority of surgeons This lack of appreciation of the condition is shown, on the one hand, by its receipt of insufficient attention and by the fact that innocent persons

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1 Sudeck, P Ueber die akute entzündliche Knochenatrophie, *Arch f klin Chir* 62 147, 1900

2 Sudeck, P Ueber die akute (reflektorische) Knochenatrophie nach Entzündungen und Verletzungen an den Extremitäten und ihre klinischen Erscheinungen, *Fortschr a d Geb d Rontgenstrahlen* 5 277, 1901-1902

3 Sudeck, P Ueber die akute (trophoneurotische) Knochenatrophie nach Entzündungen und Traumen der Extremitäten, *Deutsche med Wchnschr* 28 336, 1902

4 Gurd, Fraser B Post-Traumatic Acute Bone Atrophy (Sudeck's Atrophy), *Ann Surg* 99 449 (March) 1934



TABLE 4—*Analysis of Author's Cases*

Case No	Name	Part Affected	Year	Age	Sex	Period Lapsed Since Injury	Treatment	Result at Last Examination	Nature of Injury
1	C O	Foot	1926	34	M	2 mos	Walking plaster cast	Recovery, noncooperative	External rotation fracture of ankle, grade 1
2	V T	Foot	1927	21	M	2 mos	Hot baths	Recovery, cooperative	Subastragaloid dislocation fracture of astragalus
3	M A	Foot	1927	40	M	5 mos	Walking plaster cast	Recovery	External rotation fracture of fibula, grade 1
4	P L	Foot	1928	46	M	3 mos	Walking plaster cast	Röntgenographic evidence of recovery noncooperative (shinlrose)	Fracture of sesamoid
5	C U	Foot	1928	37	M	3 mos	Not treated	Lost from observation	Fracture of sesamoid
6	T O	Foot	1930	41	M	3 mos	Walking plaster cast	Returned to Europe recovery incomplete but favorable	Fracture of first metatarsal
7	D L	Foot	1931	42	M	5 mos	Walking plaster cast	Recovery very cooperative	Chip fracture of os calcis chip fracture of first metatarsal
8	L A	Hand	1931	35	F	6 wks	Plaster of paris cast	Not seen again	Colles fracture
9	B I	Hand	1931	49	F	5 wks	Heat, manipulation	Röntgenographic and clinical evidence of recovery	Contusion of hand no fracture
10	M G	Hand	1932	51	F	5 wks	Diathermy, active exercise	Röntgenographic and clinical evidence of recovery	Colles fracture
11	W A	Foot	1932	48	M	8 wks	Walking plaster cast	Röntgenographic and clinical evidence of recovery	External rotation fracture of ankle joint grade 3
12	T W	Foot	1932	45	M	3 mos	Walking plaster cast	Much improved	Compound fracture of great toe
13	T Q	Shoulder	1932	37	M	2 mos	Diathermy	Improving	Dislocation of shoulder fracture of tuberosity
14	W F	Hand	1933	58	M	14 mos	Not treated	Recently seen for first time roentgenographic examination showed patchy atrophy clinical examination, swelling, pain and stiffness	Contusion of hand lost from observation left Montreal

pulse pressure in the blood vessels in the neighborhood of the wrist or ankle, it appears evident that the capillaries at least are engorged and that an increase in interstitial tension has taken place

The joints become stiff, and movements, as stated before, are exquisitely painful. It is possible to stimulate dispersion of the swelling by means of posture. For this purpose, however, a comparatively prolonged period of elevation is required. With absolute rest, particularly if disappearance of the swelling is at the same time obtained, relief from pain results. In the case of the lower extremity, if unprotected weight bearing has been indulged in the whole foot may be, and commonly is, completely flattened, subluxation or, as in cases 7 and 17, actual displacement of one or more tarsal bones may be proved.

Roentgenographic examination made within a few days of the onset of the clinical phenomena previously described (as a rule within a few weeks of the date of injury) shows characteristic patchy areas of almost complete decalcification of the bones. This is most marked in the small bones of the wrist or tarsus and in the ends of the metatarsal or metacarpal bones and the phalanges. As a rule, also, it is seen that the lower end of the leg or the bones of the forearm are also involved in the atrophic processes. In the case of the shoulder, the osteoporotic process is present in both the scapula and the humerus. As the lesion progresses, the rarefaction becomes more complete so far as the small bones and the cancellous tissue of the long bones are concerned, so that the patchy appearance is lost and marked rarefaction in the shafts of the long bones also becomes evident. This is the chronic, second stage described by Sudeck.

#### INCIDENCE AND ETIOLOGY

With regard to the etiology of acute bone atrophy, there is apparently no racial influence. In my group of cases, Canadians of French and Anglo-Saxon extraction constitute the greater number. A comparable number of Jews, Italians and Central Europeans also appear. The tables will show that sex, so far as the cases involving the foot are concerned, is not of importance. The larger number of males (thirty-nine of sixty-four) is accounted for by the considerably greater incidence of injuries to the feet and ankle joints in men than in women. Very striking, however, are the facts that all of the nine cases involving the shoulder (reported from the three different clinics reviewed) occurred in men, whereas of the nineteen cases in which the hand and carpus were involved fourteen occurred in women. The absence of lesions of the shoulder in women is less easily explained, I believe, than the preponderance of cases involving the hand in women. In my experience, at least, Colles' fracture and its variants occur with considerably

however, was not done, but gradual return of function took place, so that on April 19, 1935, roentgen examination showed recalcification of bones, and movements of the foot and ankle joints had largely returned. The patient has gone back to work as a city salesman.

In my opinion the reason for the acute bone atrophy in this case was that the man was permitted to carry out weight bearing on a plaster cast which had been applied over padding. Also, destruction of the arch had been assisted by inversion of the foot at the time of first application of the cast. As mentioned previously, I believe that a more rapid and probably better ultimate result would have been obtained if protected weight bearing had been persisted in for a longer period.

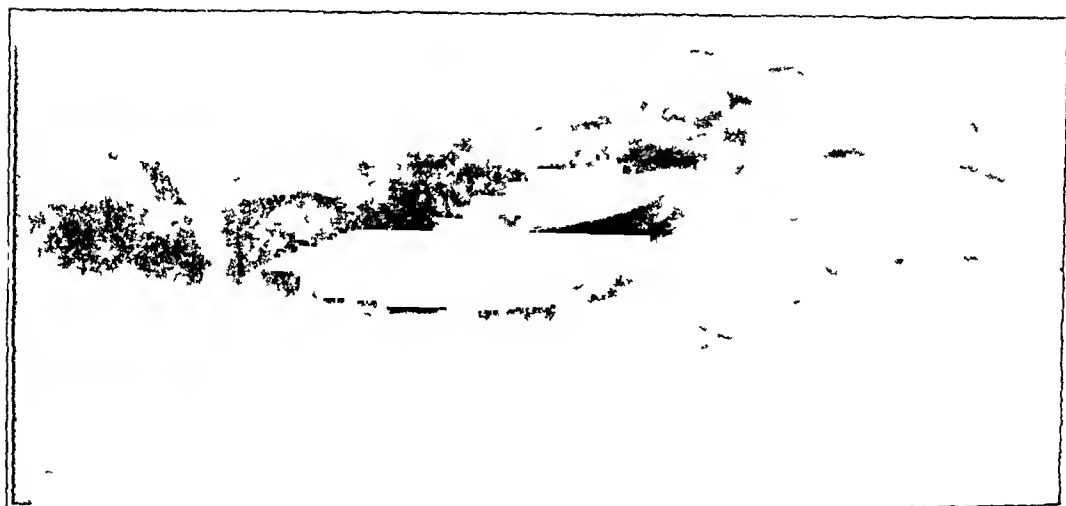


Fig 2 (case 17) —Roentgenogram showing the second stage of acute bone atrophy associated with marked subluxation of the bones of the tarsus

CASE 19—L. A. was injured on July 13, 1934, when she fell on the flexed wrist. She did not receive any treatment until approximately twenty-four hours after the accident. During the interval she drove a considerable distance (60 miles) by road to the hospital. Roentgen examination showed a fracture of the reversed Colles or Smith type. Reduction was accomplished with the patient under anesthesia, the limb was placed in supination, and moderate dorsiflexion was employed at the wrist joint. There was no immediate swelling and no considerable amount of pain. Progress was satisfactory until one month after injury, when the hand, which was still in a plaster cast, somewhat suddenly became swollen and the joints of the fingers painful on movement. In the interval, the fingers had been continuously exercised and the hand employed for activities not requiring any considerable strength. Roentgen examination made on September 22 showed marked acute bone atrophy. The patient was advised to refrain from any movements of the forearm, wrist or hand which might cause pain. Diathermy was employed and hot bathing at home. By January 1935 the condition was markedly improved clinically, and roentgenographically recalcification seemed to have taken place.

pathologic or unstable condition of the nervous system or of the general circulatory system is in any way responsible

Hitherto, unfortunately, the actual pathologic process of the condition has been subjected to few investigations, and unless one accepts the experiments of Pavlov (as reported by Noble and Hauser) by which he produced softening of the bones in dogs by continuous application of damp and cold to the extremities, a comparable lesion has not been produced experimentally in animals. The histologic examination



Fig 1 (case 20)—Roentgenogram showing patchy osteoporosis six months after fracture of the clavicle. The patient suffered extreme pain

of specimens by Vialleton and by Fontaine and Herrmann show that there is a marked diminution of the number and thickness of the bony lamellae in the osteoporotic hand. The absorption of bone is apparently not the result of osteoclastic activity since the specific phagocytes are not seen in any of the preparations. These studies also appear to prove that there is a uniform loss of bony substance and not merely a depletion of the mineral salts of the bone.

The actual reason for the bone absorption must, I believe, be presumed to be hyperemia. An attempt to discover the cause of the

When the patient was last seen on April 1, except for a slight deformity due to volar tilting of the articular surface of the radius, function of the hand, wrist and forearm was substantially normal

Unless the fact that during the first twenty-four hours following injury this injured extremity was subjected to considerable trauma, owing to delay in reduction and fixation, explains the onset of acute bone atrophy, I am at a loss to explain the exhibition of the phenomenon in this case

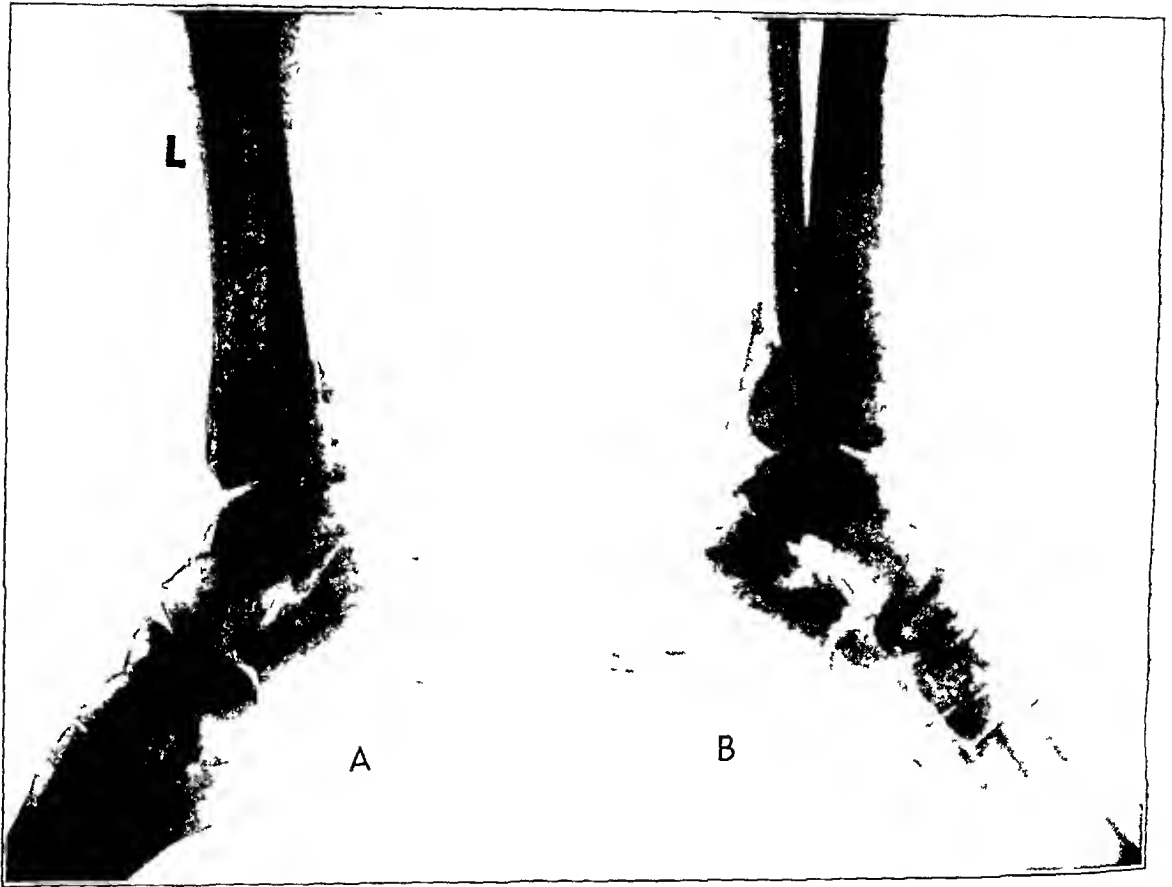


Fig 4 (case 23) —The patient was injured on Oct 27, 1934. *A* is a roentgenogram made on December 11. Note the absence of atrophy of the bone after six weeks' disuse. Second injury occurred on Jan 23, 1935. *B* is a roentgenogram taken on February 7. Note marked patchy bone atrophy two weeks after repetition of trauma.

During February 1935, Dr Gaylord S Bates, of Detroit, sent me the roentgenograms and history concerning the following case:

CASE 23—B O., aged 57, fractured the right ankle joint (external rotation, type III) on Oct 27, 1934. Reduction was carried out, and a circular plaster cast

In four of the seven cases of acute atrophy involving the foot and tarsus the lesion was due, I believe, to too early unprotected weight bearing with consequent repeated trauma to injured tissues

In one case (case 23) I am of the opinion that the patient suffered a second injury to a previously fractured ankle joint a few days before the development of the acute atrophy and that it was this second injury which was responsible for the atrophy. In the case of involvement of the shoulder (reported in this series) incomplete fixation with too great activity on the part of the patient, with consequent repeated minor trauma, is indicated by the history

So far as prophylaxis is concerned, it appears that early adequate reduction and fixation, and so protection of the tissues from repeated trauma, are of prime importance. Also it appears that in each individual case the surgeon must attempt to decide whether for a patient already subjected to manipulative measures the risk of acute bone atrophy must not be balanced against possible improvement in position by further intervention. The case reported by Greig and case 10 in my first series are significant in this connection

A table based on the fourteen cases described by me in 1934<sup>4</sup> is republished here by courtesy of the *Annals of Surgery*, and a further tabulation of ten cases has been prepared (tables 4 and 5). Brief reports of five cases follow. It will be noted that in four of these cases the fact of continued or repeated insult to the tissues is exemplified

#### REPORT OF CASES

CASE 17—B E, aged 42, was injured on Dec 28, 1933, the medial malleolus being fractured. A plaster of paris cast was applied in the orthopedic department over padding. The patient was advised to walk on the plaster, to which a metal stirrup was applied. The cast was removed on May 5, 1934. On May 12 marked swelling developed, accompanied by great pain and immobility of the foot and ankle. The patient had walked a little since removal of the cast, and marked flattening of the foot had occurred, with astragaloscaphoid subluxation. Roentgen examination on May 12 showed marked acute bone atrophy and complete loss of the arch to the foot (fig 2). The patient was admitted to the hospital, the edema disappeared when the proper posture was employed, assisted by baking. An unpadded plaster of paris cast up to knee and a felt heel<sup>10</sup> were applied, the arch of the foot was reproduced. The patient walked well in the unpadded cast with little pain. The cast was removed on September 11. Roentgen examination showed marked improvement, and the appearance of the foot was much improved, though it was still swollen and tender. The arch of the foot was considerably improved, but the joints of the ankle and foot were stiff. I believe that a plaster cast should have been reapplied. This,

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10 Gurd, Fraser B. Treatment of Fractures Involving the Ankle-Joint with Special Reference to the Use of the Pillow Splint and Early Weight-Bearing, *Ann Surg* 88 260 (Aug) 1928

the most familiar examples of such osteoporosis is that seen after Colles' fracture, as a roentgenogram taken a week or ten days after the injury may show decalcification of the cancellous extremities of all the metacarpal bones and the phalanges

He published a picture which is an example, I believe, of the condition forming the subject of this essay. The history, also, is that which is to be expected in cases of acute bone atrophy



Fig 5 (case 24)—Roentgenographic appearance two months after a needle puncture wound of the tarsus

A female post-office telegraphist, aged 41 years, sustained Colles' fracture of the left arm, and the nature of the injury being overlooked, healing took place with such deformity as to incapacitate her entirely for her duties. Two months later a roentgenogram showed the bones of normal consistency. The malposition of the displaced fragment was rectified by open operation and after a week's interval a roentgenogram showed a localized decalcification of the carpus, the distal extremities of the radius and ulna and of the contiguous extremities of all the metacarpal bones and phalanges.

TABLE 5—Analysis of Author's Second Group of Cases

Case No	Name	Part Affected	Year	Age	Sex	Nature Injury	Period Elapsed Since Injury	Treatment	Result	Apparent Cause of Atrophy
15	W H	Hand	1925	51	M	Colles' fracture very severe	6 wks	Physical therapy, manipulation	Poor after 18 mos ultimately fair	24 hr delay in reduction without fixation
16	L A	Foot	1933	41	M	Fracture B B leg	5 mos	Graduated exercise, physical therapy	Fair work in 13 mos	Injury to knee joint over bearing
17	B L	Foot	1933	42	M	Fracture of medial malleolus	5 mos	Walking plaster cast	Good	Early unprotected weight bearing
18	O H	Foot	1933	35	M	Fracture of tibia, middle and lower thirds	6 mos	Walking plaster cast	Good	Too early unprotected weight bearing, subas tragaloid injury over
19	L A	Hand	1931	50	F	Reversed Colles' fracture	2 mos	Rest, diathermy	Cure after 5 mos	Delay in reduction and fixation
20	E M	Shoulder	1934	50	M	Fracture of clavicle	2 mos	Rest, diathermy	No important result in 10 mos	Incomplete and too short fixation
21	V F	Foot	1934	40	M	Fracture of scaphoid	10 wks	Rest physical therapy	Fair after 6 mos	Incomplete fixation, unprotected weight bearing
22	R O	Foot and ankle	1931	44	M	Fracture of tibia	4 mos	Graduated exercise	Cure after 2 mos	Too early unprotected weight bearing
23	B O	Foot	1931	57	F	Fracture of ankle joint grade 3	8 wks		Not known	Second injury before firm union
24	M O	Foot	1934	40	M	Needle puncture	2 wks	Physical therapy	Good after 2 mos	Injury to tarsal joints



by rather better results. In the case of the lower extremity, I am convinced that the unpadded walking plaster cast, which is applied after absolutely all interstitial edema has been disposed of and to which a felt heel has been added is the method of choice. If care is applied to remodel the foot, particularly with reference to overcoming pronation and flattening of both arches and if the patient walks sufficiently, the results are satisfactory.

I have had experience with sympathectomy as recommended by Fontaine and Heirmann in but one case. In this case the result was not favorable, at the same time the evidence which these authors supply cannot be ignored.

### ABSTRACT OF DISCUSSION

DR E W RYERSON, Chicago. Sudeck's atrophy has a tremendous bearing on cases involving compensation, insurance, etc. A study of the condition will clear up questions of malingerism to a high degree.

I have seen a number of cases of this particular variety of atrophy, and it is extremely troublesome. Only comparatively recently have I become aware of the existence of Sudeck's atrophy as a clinical entity. No one knows the exact cause. Dr Gurd pointed out an extremely important feature, that while the roentgenogram demonstrates definite atrophy of the bone, it does not demonstrate what I am sure is equally present, great atrophy of the ligamentous structures. The case presented by him in which the foot was involved was very convincing because the flattening of the arch was due not to the bone atrophy, as the bones remained intact, but to the ligamentous atrophy, which, unfortunately, had not been well shown by any of the pathologic reports.

It is unfortunate that in so many cases it is necessary to use plaster of paris to immobilize the affected joints sufficiently. Plaster of paris is distinctly inhibitive to the formation of bone. Calcium is absorbed in the bones when circular plaster of paris casts are applied, and it is unfortunate that splints or plaster casts with windows cut in them cannot be used more uniformly, so that the treatment which I believe to be extremely important, that with sunlight or imitation sunlight, can be applied. The giving of large doses of calcium in any of the newer forms might be of advantage, but rest is the main feature of importance.

The use of sympathectomy or interruptions of the autonomic nervous system seems to me to be contraindicated in cases of Sudeck's atrophy, because there is already too active a circulation. The word "anxiety" was new to me. I therefore went to the exhibit downstairs and looked into the two largest medical dictionaries, neither of which features "anxiety." I judge that it means an excessive amount.

One more feature is that in most of these cases the atrophy is confined to the bones making up the affected joints and not to the diaphyses or any other bones in the skeleton, this shows that this unusual and interesting disease is not connected in any way with involvement of the parathyroid glands.

DR ROBERT V FUNSTEN, University, Va. Since hearing Dr Gurd's paper I have a clearer understanding of posttraumatic acute atrophy of the bone than I have ever had before. He has gone carefully through the chronological development of this particular syndrome into a clinical entity and has established a

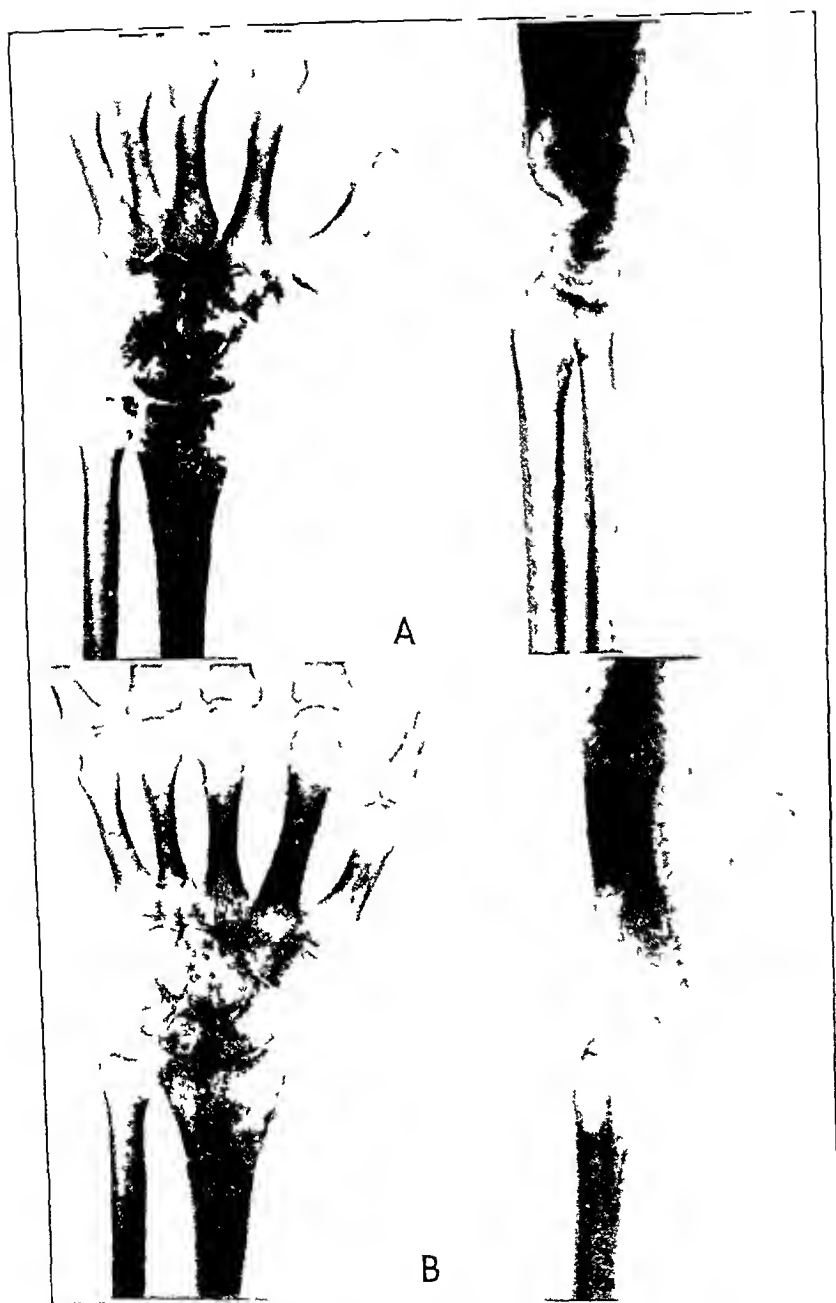


Fig 3 (case 19) — *A*, roentgenogram showing the original conditions before reduction, *B*, view showing marked patchy osteoporosis two months after injury

ment except the one which I believed would cure him, and finally had the arm amputated

CASE 3—A woman about 50 years of age had had her shoulder moved, under gas anesthesia, to break up adhesions. About six weeks later, while she was still wearing an aeroplane splint and receiving physical therapy, osteoporosis developed in the hand. Rest, heat and medication for what was thought to be arthritis gave no relief. In this case the roentgenogram revealed the true condition. Sympathectomy gave complete relief from pain.

CASE 4—A woman about 65 years of age suffered Colles' fracture. Reduction was good, and she made uneventful progress. Soon after the cast was removed, swelling, changes in color and other signs of osteoporosis developed. A roentgenogram showed osteoporosis, but also that union of the fracture was not complete. Replacement of the splint gave relief, so did heat and massage. These measures were carried out with complete cure.

CASE 5—A woman, aged 50, received a small chip fracture in September. She was first seen early in November. Roentgenographic changes were slight, but the clinical picture was marked. Sympathectomy was done, and relief was almost instantaneous, but swelling and color changes subsided slowly. However, four months later there was complete cure clinically. My associates and I have found almost invariably that the patient has discovered some position in which he holds the limb in an attempt to get relief. This position differs with each patient.

#### ABSTRACT OF DISCUSSION

DR PHILIP LEWIN, Chicago. I want to ask Dr Gurd whether cold applications or local anesthesia have any place in the prophylactic treatment of this lesion.

DR FRASER B. GURD, Montreal, Canada. I am sure that all appreciate that I purposely avoided discussing treatment, and, with permission, I shall continue to side-step this question, apart from reiterating again my conviction that any form of treatment which is accompanied by pain, or would be accompanied by pain if an anesthetic were not used must be avoided at all costs.

Although this is the place, there is not, I believe, the time to discuss Dr Ryerson's question as to the use of plaster of paris casts. I prefer the use of circular plaster of paris casts as an immediate treatment of most fractures below the knee.

"Nimety" is a word used by Greig. It is defined in the Oxford dictionary and does, as Dr Ryerson assumed, mean excess or redundancy. I assumed that perhaps others might not know the meaning of the word "nimety," consequently I always use the word "hyperemia" at the same time when talking of "nimety" of the blood supply.

With regard to Dr Funsten's case, I am not sure as to the diagnosis. One important bit of evidence one would like to know in connection with it is the extent to which the patient ultimately recovered function and the length of time required for that condition to be brought about.

Dr Carothers' presentation was so complete in itself that I do not think that there is any particular reason for my taking up the matters discussed by him, unless it were the question of sympathectomy, and, as I have already indicated, I do not believe there is time at the present moment to discuss it.

In the case presented by Dr Carothers in which there was typical moth eaten, flaky atrophy of osteomyelitis of the tibia, I refer again to my first remarks in

was applied, which was bivalved six weeks later. Roentgen examination was made on December 11. The picture showed no evidence of important decalcification. Physical therapy was employed for four weeks, and at the end of ten weeks from the date of injury weight bearing, with crutches, was allowed. At this time, full, free and painless motion was present and but little swelling. Clinically, alignment was perfect. On Jan. 24, 1935, the patient received a five hour treatment in the fever machine on account of cerebrospinal syphilis. On January 23 she turned her ankle, she suffered pain at the time but thought nothing of it. On January 25 there was severe pain in the ankle and foot, with considerable swelling and some darkening of the skin. When the patient was seen by Dr. Bates two weeks later, the foot and ankle were very much swollen, and she complained bitterly of pain, the foot at that time was quite obviously pronated. Roentgen examination made on February 7 showed deformity and marked patchy bone atrophy.

Dr. Bates in his letter to me stated that the question of Sudeck's atrophy had been immediately considered when the roentgenograms were examined, exhibiting as they did the picture of patchy osteoporosis associated clinically with intense pain, swelling and loss of function. I believe that the injury reported by the patient as having occurred on January 23 was more likely to have been responsible for the onset of the condition than the use of the fever machine. The pictures taken in January show moreover, that the almost perfect reposition of fragments shown had been lost.

Dr. R. C. Moehlig, of Detroit, furnished the description and roentgenograms of a very interesting case.

CASE 24.—On June 24, 1934, a syringe with a long needle fell on the foot of the patient, aged 46, and the needle penetrated the foot between the tarsal bones for at least 2 inches (5 cm.). The same evening the patient suffered a chill and marked pain in the foot. The pain became very severe,  $\frac{1}{2}$  grain (0.032 Gm.) of morphine being required to relieve it, and the swelling increased for about a week. The skin became shiny, and later cyanosis developed. Two weeks after injury roentgen examination, made with a portable unit, revealed rather marked osteoporosis of the tarsal bones next to where the needle had entered. On August 20 further roentgen examination showed well marked, patchy bone atrophy, involving all the bones of the tarsus, the metatarsus and the phalanges (fig. 5). Physical therapeutic measures were instituted, and one month later pain in the foot was slight and was improving, the swelling was lessening and the normal pink color had returned to the foot.

Although Greig<sup>11</sup> did not use the expression acute bone atrophy, or any comparable term, he did refer to the fact that comparative hyperemia in disused bones may be not a purely passive phenomenon but an active one—one which is reflex through the autonomic nerves bringing about an active dilatation of the blood vessels. He stated that one of

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11 Greig, David M. Clinical Observations on the Surgical Pathology of Bone, Edinburgh Oliver & Boyd, 1931.

# EARLY ASYMPTOMATIC ACOUSTIC TUMOR

REPORT OF SIX CASES

MARY HARDY, D Sc

AND

S J CROWE, M D

BALTIMORE

In Cushing's<sup>1</sup> book "Intracranial Tumours," published in 1932, the term "acoustic tumour" was used to describe the growth which originates in that portion of the acoustic nerve which lies within the internal auditory canal. Dr. Cushing stated that histologically such a tumor resembles those seen in other parts of the body in Recklinghausen's disease, that it is probably congenital and that clinically a loss of vestibular response to caloric tests is an early objective sign which precedes complete loss of hearing.

As an acoustic tumor increases in size, the nerves in the internal auditory canal (cochlear, vestibular, facial and intermediate nerve of Wrisberg), together with the internal auditory artery, which is the main source of blood supply for the inner ear, are compressed against the bony wall of the canal, and an increasing impairment of function results. Indeed, the pressure of the growing tumor often enlarges the auditory canal, this is sometimes seen in roentgen films. An acoustic tumor may grow toward the brain stem, occupy the cerebellopontile angle and give rise to symptoms caused by involvement of other cranial nerves. Cushing made a distinction, however, between the acoustic tumor which originates from the nerves deep in the auditory canal and the cholesteatoma, glioma and other types of new growth that may occupy the cerebellopontile recess.

In our investigation of the middle and inner ear, we have since 1924 been collecting and making serial sections of temporal bones, in order to correlate histologic structure with antemortem clinical tests of hearing and vestibular function. The tests for hearing are made with the Western Electric 1-A or 2-A audiometer, tuning forks and the voice. When the patient is not too ill the tests are made in a sound-proof room. Masking is used to insure that the record of hearing for each ear is accurate. The only studies on vestibular function have been

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From the Otological Research Laboratory of the Johns Hopkins University

<sup>1</sup> Cushing, H. Intracranial Tumours, Springfield Ill., Charles C Thomas, Publisher, 1932

## COMMENT

Watson Jones and Roberts<sup>12</sup> published reproductions of roentgenograms made in two cases of Colles' fracture (p 468, fig 314). One of these pictures shows marked patchy bone atrophy, particularly of the carpal bones and the ends of the metacarpals. They expressed the opinion that decalcification in this case was due to disuse of the limb, since it had been immobilized by splints, whereas in the other case the extremity had been so fixed in plaster of paris that function of the hand had not been seriously interfered with. I believe that the authors' statement of the reason for this decalcification is not correct, and I am of the opinion that the one case was, in fact, an example of acute bone atrophy, although the reason why the condition should have occurred in this case is not evident, as no history is given.

In April 1934 a contribution by Donald Gordon of New York appeared under the title "Disability Due to Swelling Following Trauma of the Extremities." Gordon and I agree that the disability which follows in certain traumatic cases is associated with swelling, we differ, however, as to the relationship. Gordon believes the swelling to be the primary cause of the changes which are set up in the limb, whereas I am of the opinion that this phenomenon is one of the more easily demonstrated results of the presence of those changes which have been described under the heading of posttraumatic acute bone atrophy. Another essential difference in the views of Gordon and myself is that whereas the former believes that ischemia is responsible for initiating the condition, in my opinion the evidence seems to prove that excessive circulation, or to use Greig's terminology, a nuxiety of blood supply to the part, is the essential primary cause.

The results of treatment appear to prove that the process of acute bone atrophy is reversible, the length of time required to bring about clinical cure is likely to be prolonged for from six months to an even longer period. With reference to treatment, I believe that the most important memorandum is that pain should be avoided and, more particularly, that anything in the nature of forcible manipulation, either with or without an anesthetic, should be excluded.

In the case of the upper extremity, if further insult to the tissues is avoided the course is toward repair. The patient should be warned that no painful movements of any sort should be undertaken. I have employed both snugly fitting unpadded plaster casts and physical therapeutic measures especially diathermy with hot bathing at home. The latter procedure, as a rule, pleases the patient better and also is followed

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<sup>12</sup> Jones, R. Watson, and Roberts, R. E. Calcification, Decalcification and Ossification, *Brit J Surg* 21 461 (Jan) 1934.

case (fig 13) there was a growth on each side that seemed to arise from the meninges (meningioma). The tumor in the remaining case (fig 14) differs from all others we have seen in this locality in that it contains glial tissue and large nerve cells. Dr. Adolf Meyer expressed

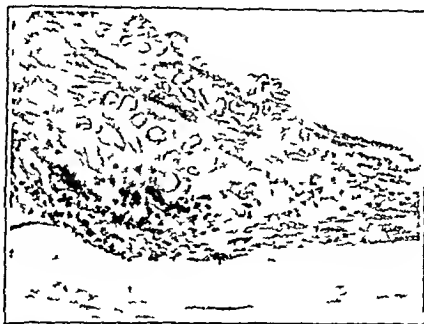


Fig 2—Photomicrograph of a section through an angiomatous network of blood vessels in the ganglionic region of the inferior division of the vestibular nerve,  $\times 24$

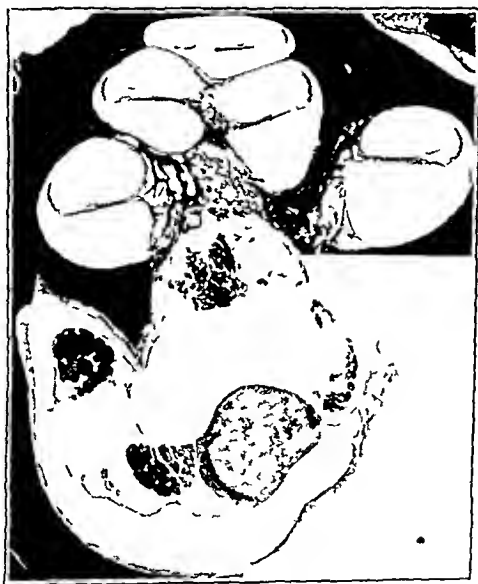


Fig 3 (case 1)—The inferior division of the vestibular nerve is seen in this section as spread out in a crescent-shaped band on the side of the tumor. The other nerves and the inner ear were normal,  $\times 7$

the opinion that the growth originated from misplaced sympathetic ganglion tissue.

An angiomatous-like network of blood vessels, similar to that shown in figure 2, was observed in three of the cases in which a tumor was present and in seven others of the 250 cases in which examination

clear clinical, diagnostic and etiologic standard for the disease. As I review from memory cases which I recognize now to have been instances of posttraumatic acute bone atrophy, I wish that I could have had the advantages of Dr Gurd's suggestions as to treatment.

My impression has been that there were two types of the disease—one occurring within two or three weeks after injury and showing rather extensive changes in the calcium in the affected bones and the other occurring at a later period after injury. Concerning the former, I should like to show a roentgenogram that was taken of a man 65 years of age three weeks following his injury. This roentgenogram shows extensive decalcification with blurring of the structure of the bones, which was not present in the roentgenogram taken at the time of his injury. In this roentgenogram calcified vessels may be seen also which seemed significant to me. Dr Gurd considers hyperemia to be one of the etiologic factors. I should like to ask him if the reversal of this could also produce similar changes in bone from this cause rather than the ischemia which develops as a result of swelling, as suggested by Greig.

DR RALPH G. CAROTHERS, Cincinnati. In the fracture service at the Cincinnati General Hospital Dr Herrmann advises sympathectomy in most instances, whereas Dr Gurd has used nonoperative methods in his cases. The discrepancy of these two points of view is more apparent than real. There are many persons with post-traumatic osteoporosis who will get well without treatment. Physical therapy will without doubt cure many others, but sympathectomy in cases accompanied by great pain will, I believe, relieve the pain earlier and certainly hasten the cure. Thirty-seven cases have been referred to Dr Herrmann in thirty months, but he operated only on the younger patients of this group. The average time at which these patients returned to work was three months. The others, whose general condition and age contraindicated operation and who were treated by physical therapy alone, were slower in recovering, though in most cases the condition was of the milder type to begin with. The patients operated on were those who suffered from a painful swelling which was made worse by splinting and rest and was unrelieved by physical therapy. These were patients who had torn off splints and for whom casts had been changed and all manner of measures had been carried out in an attempt to give relief from pain. As the pain was of visceral origin, it was difficult to obtain relief except with the administration of morphine. Furthermore, by the uninitiated the reason for the pain cannot be appreciated, and many patients have been unjustly tagged malingerers. A few cases will illustrate my point.

CASE 1—The patient did not suffer from acute painful posttraumatic osteoporosis and had no swelling, changes in color and no pain in the foot. However the roentgenogram showed marked osteoporosis of the foot, which had followed a compound fracture of the tibia with infection.

CASE 2—A young man was seen six weeks after a fracture of one of the small bones. The position of the fragments was perfect, but the roentgenogram showed marked osteoporotic changes. There were some swelling, typical changes in color and great pain. The pain had been present since the injury, and the patient had gone from one physician to another seeking relief. Splinting had been ineffectual, so had diathermy, infra-red rays and massage. I advised operation on the brachial artery, which the patient refused. He was not seen again, but I have learned that he went from one office to another, trying every sort of treat-



with the audiometer, tuning forks and the voice, made by Dr C C Bunch, showed normal hearing in both ears. On account of the patient's condition and in the absence of either vertigo or nystagmus, a caloric test was not made.

The growth was on the left side and arose in the inferior division of the vestibular nerve. It was about 25 mm at its greatest diameter. There was no evidence of a new growth on the right side. The involvement of the nerve and the size of the tumor in relation to the size of the internal auditory canal at this point is shown in figure 3. In figure 4 the growth is seen invading the ganglion of the inferior division of the vestibular nerve. The location of the growth and its relation to the other nerves are shown in figure 5.

In this patient a new growth, which invaded a branch of the vestibular nerve, did not give rise to subjective or objective clinical symptoms. The growth for the



Fig 6 (case 2)—At the level of this section, through Scarpa's ganglion, both divisions of the vestibular nerve were infiltrated by tumor cells, and by the angiomatous network of blood vessels,  $\times 7$

most part was outside the nerve, but it was not attached to any of the adjacent structures.

**CASE 2**—A man aged 64 had bilateral adrenal tumors (neuroblastoma) and died of pneumonia about two weeks after operation. When his hearing was tested, in November 1930, the patient was ill and very emaciated. Neither tuning fork nor vestibular tests were made, but the tests with the audiometer showed hearing to be within the limits of normal on both sides. The patient had never had vertigo, and nystagmus was not observed.

The growth was on the left side. It had invaded both divisions of the vestibular nerve, as shown in figures 6, 7 and 8. Some of the ganglion cells in Scarpa's ganglion had been destroyed. This was one of the cases in which both a tumor and an extensive angiomatous network of blood vessels in the nerve were observed. The greatest diameter of the growth was 5 mm. The tumor did not involve the cochlear nerve. When the brain was removed the nerves in the internal auditory canal of the opposite side were pulled out, so we have no definite information as to whether the tumor was unilateral or bilateral.

quoting Sudeck's titles of his first two original articles. This condition unquestionably occurs in any condition in which there is "nimiety" of the blood supply, or hyperemia, whether due to staphylococcic or tuberculous infection. But the problem being discussed is why one sees similar conditions in cases in which there are no tumors or acute inflammatory change with its accompanying "nimiety" of blood supply.

In regard to the use of cold applications and local anesthesia, I do not know whether cold applications are valuable and I have had no experience with local anesthesia.

or the cochlear nerve but was attached to both. We are unable to determine the exact point of origin. In this case there was also a network of blood vessels in the neighborhood of the tumor (fig 10).

The patient was an old man with a very small tumor, which either had been present for a short time or had had an exceedingly slow rate of growth. Mitotic figures were not seen in the sections of this or any of the other tumors reported on in this paper.

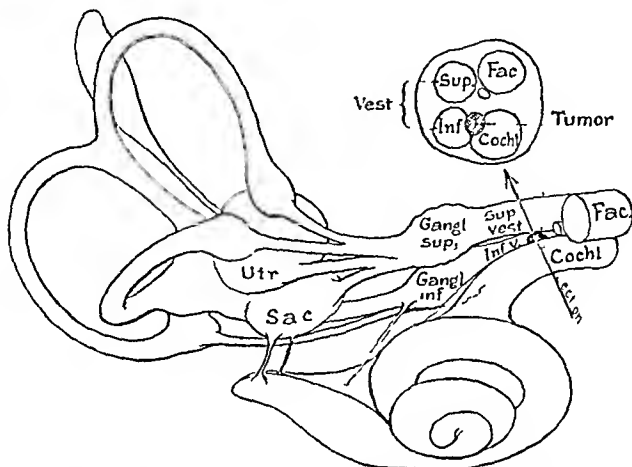


Fig 9 (case 3)—This very small tumor was located between the cochlear nerve and the inferior division of the vestibular nerve proximal to Scarpa's ganglion.



Fig 10 (case 3)—This section passes through the greatest diameter (0.7 mm) of the tumor, and shows its close relationship to the cochlear nerve and to the inferior division of the vestibular nerve,  $\times 7$ .

CASE 4—A white woman aged 61 died in April 1931 of chronic nephritis and hypertension. The general condition of the patient, who was on the verge of uremia, was such that complete functional tests were not made. The audiometer test showed that the hearing was the same for both ears, and the vestibular caloric test caused a normal response on each side.

made with the caloric test. Approximately eight hundred pairs of temporal bones have been collected and sectioned. A detailed study of serial sections in two hundred and fifty unselected cases disclosed that in six there was an acoustic tumor which did not give rise to clinical symptoms. The tumors were so small and so deep in the internal auditory canal that they were overlooked at autopsy and at the time the gross specimens were described in the laboratory.

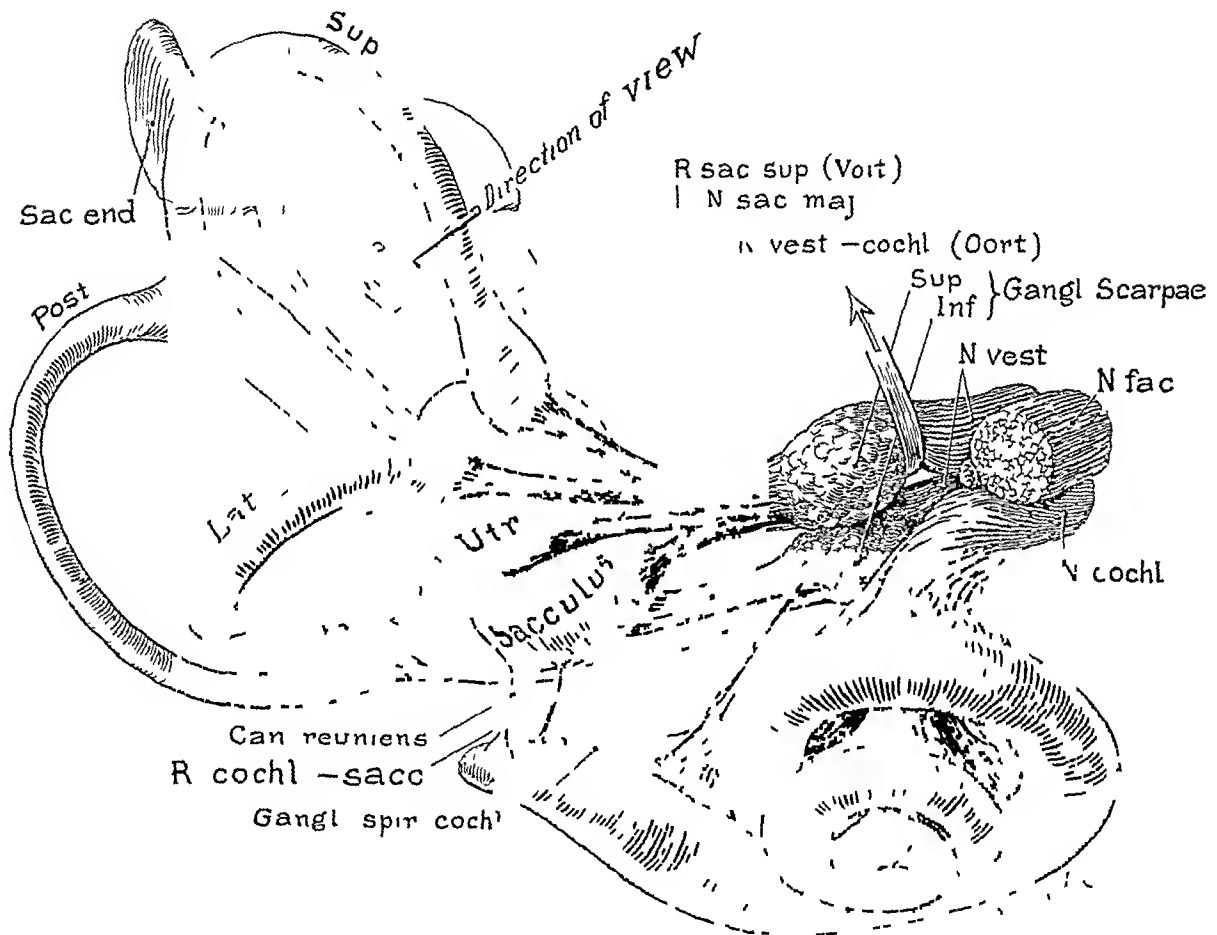


Fig 1—A semi-diagrammatic drawing of the human labyrinth and its innervation, showing especially the branching pattern of the vestibular nerve (Hardy, *M. Anat. Rec.* 59 403, 1934). Reference should be made to this representation of the normal condition in studying figures 5, 8, 9, 11, 13 and 14.

The diagrammatic drawings show for each case the size of the tumor, its point of origin and its relations to the nerves in the internal auditory canal as determined from the serial sections. In four of the six cases the tumor arose in the vestibular nerve (figs 5, 8, 9 and 11). In one

nerve The growth seemed to arise from the dura covering the bony ridge (crista transversa), which separates the cochlear from the facial nerve It was difficult to make this relationship clear in the drawing (fig 13) The sections showed that the growth passed downward across the fundus of the internal meatus from its attachment to the dura and involved a few small bundles of the cochlear nerve just before they entered the cribriform plate Histologically the tumor cells resembled those seen in the tumors previously described

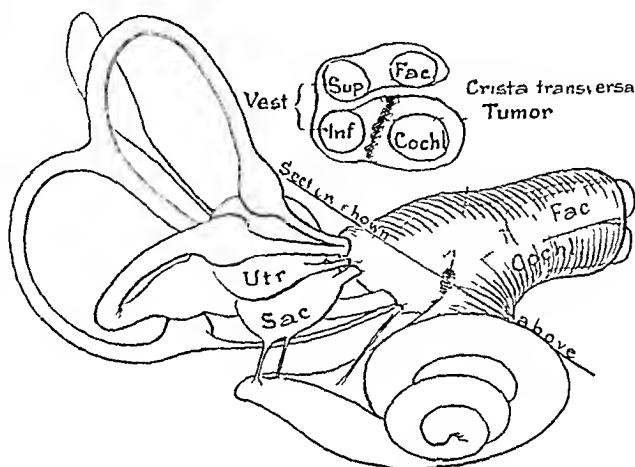


Fig 13 (case 5) —This elongated small tumor, attached to the dura mater covering the crista transversa, involved a few bundles of cochlear nerve fibers, these are too small to be represented in the drawing The dura of the internal auditory canal is schematically shown in this drawing

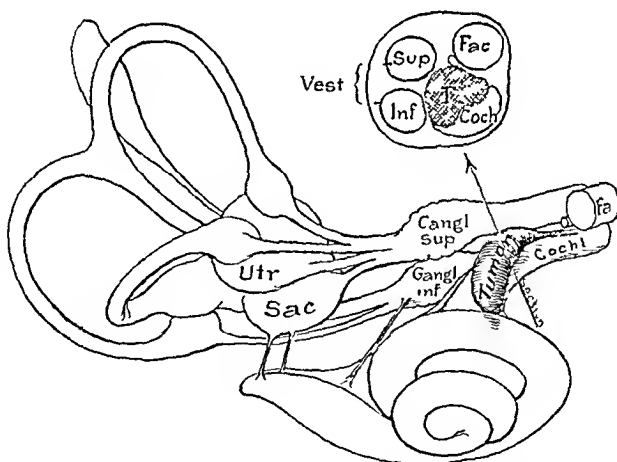


Fig 14 (case 6) —This tumor, which differed histologically from the other five, pushed aside part of the cochlear nerve but did not invade its substance

CASE 6—A Negro aged 28 was admitted to the Baltimore City Hospital (Bay View) with advanced pulmonary tuberculosis The Wassermann reaction was positive The patient had never had difficulty with his ears The audiometer test, made by Dr C C Bunch in March 1929 (one month before death), showed hearing within normal limits The reactions to the tuning fork test were also normal Vestibular tests were not made

was made. As a rule this vascular network lies in or around the vestibular rather than the cochlear or facial nerve. No evidence of vestibular irritation was noted in any case in which a tumor or a network of blood vessels in the nerve was observed.

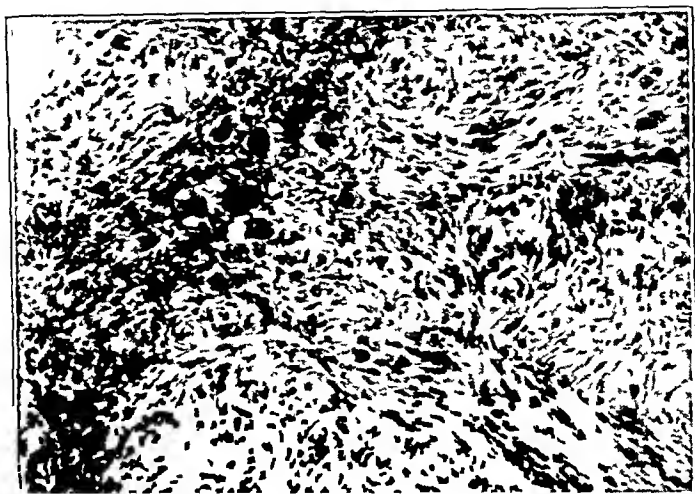


Fig 4 (case 1) —The invasion of the vestibular nerve in the region of Scarpa's ganglion is well seen at this magnification ( $\times 130$ ). Histologically the tumor was identical with large acoustic tumors that give rise to severe symptoms.

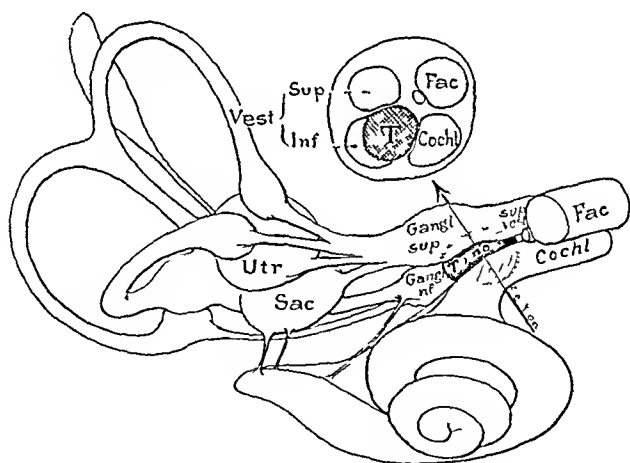


Fig 5 (case 1) —This and the other outline drawings (by Max Brodel) show the location and the approximate size of each tumor in relation to the labyrinth as a whole. (For complete labeling of the parts, see figure 1.)

#### REPORT OF CASES

CASE 1 — A Negro aged 30 was admitted to the medical service of the Johns Hopkins Hospital in October 1928, with syphilitic aortitis and hypertension. The patient made a definite statement that he had had no vertigo or tinnitus. Tests

# SURGICAL TREATMENT OF CHRONIC ULCERATIVE COLITIS

WITH SPECIAL REFERENCE TO APPENDICOSTOMY OR CECOSTOMY  
TUBE IRRIGATION

CARL A KUNATH, M D

IOWA CITY

Twenty years ago ulcerative colitis was considered a disease belonging exclusively in the field of internal medicine, and the surgeon was called on to treat only certain complications that arose. The treatment of the disease process itself by surgical procedures is, relatively speaking, still in its infancy and has not yet reached the stage of universal acceptance. If one follows the history of the subject one sees surgical procedure after surgical procedure rise with a wave of enthusiasm only to be forced into the background by some innovation in medical treatment. The large number of methods of attack in use today, together with the high mortality that still prevails, make it obvious that the ideal method of treatment has not yet been discovered.

In general, the surgical procedures that have been developed aim at one of three things: (1) to provide an avenue for direct irrigation of the diseased bowel (e g, appendicostomy), (2) to establish a condition of physiologic rest for the diseased bowel by diverting the fecal stream (e g, ileostomy), (3) to eradicate the disease by total or partial colectomy. On the whole, the results have been far from encouraging, and the tendency has been for the surgeon to advise more and more radical procedures earlier in the course of the disease. In reviewing the literature on this subject it seems that ileostomy is the treatment accepted in most of the leading clinics dealing with this disease. However, colectomy appears to be gaining favor rather rapidly.

For reasons to be discussed later, we in this clinic have, during the past four years, treated a number of patients for chronic ulcerative colitis by a more conservative form of therapy, namely, the establishment of an appendicostomy or a cecostomy with subsequent irrigation of the diseased bowel through a tube. This is by no means a new procedure, but it has provided a convenient method of comparison with the more radical procedures and has enabled us to draw a few conclusions about the disease in general.

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From the Surgical Service of the University Hospitals, University of Iowa

In this patient there was extensive involvement of both divisions of the vestibular nerve at the level of Scarpa's ganglion, but clinically there was no evidence of vestibular irritation

CASE 3—A Negro aged 78 in December 1929 was admitted to the medical wards of the Baltimore City Hospital (Bay View) with chronic myocarditis and senile dementia. It was difficult to obtain a reliable history or to make

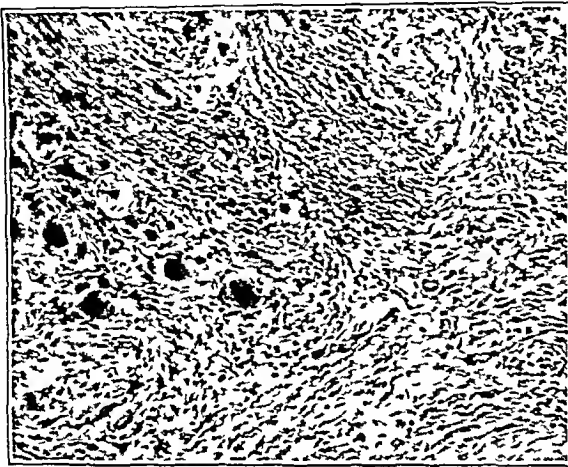


Fig 7 (case 2)—This is a portion of the section shown in figure 6 at higher magnification,  $\times 130$ . This area shows normal nerve fibers and ganglion cells in close relation to the tumor cells.

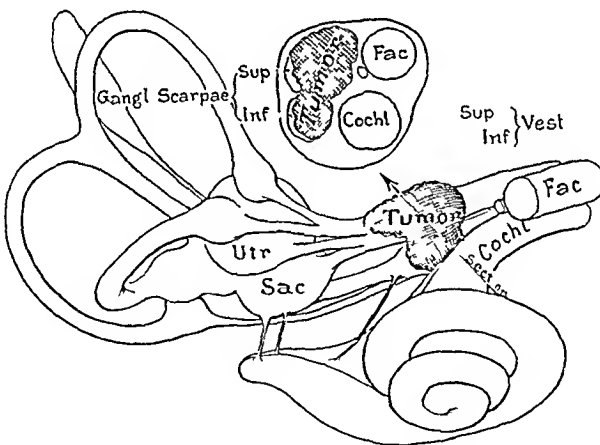


Fig 8 (case 2)—The greatest diameter of this, the largest of the six tumors, was about 5 mm.

accurate tests of hearing. The responses to vestibular caloric tests, however, were normal on both sides.

The tumor was on the right side and was less than a millimeter in diameter. It lay between the cochlear nerve and the anterior division of the vestibular nerve as is shown in figures 9 and 10. Histologically it was identical with the growth in case 1 (fig 4). The growth had not invaded either the vestibular



or some time after returning home. The mortality rate for the entire group is 46 per cent. There were ten early deaths, which occurred from one to twenty-four days following operation, the average interval being eleven and one-third days. Permission to perform an autopsy was secured in seven of the ten cases. Peritonitis stood first as the cause of death, being the diagnosis in 70 per cent of the cases. In four cases the peritonitis was generalized, in three it was localized with abscess formation. Definite perforation of the bowel was found in only two cases, in another there was a perforation of the bladder. Other causes of early death were pulmonary infarction and bronchopneumonia. In one case in which permission to perform an autopsy was not granted death was probably due to general debility, and depletion from the colitis itself.

There were six late deaths, which occurred from seven months to four and one-fourth years after operation, the average interval being

TABLE 2—*Mortality Classified as to Various Operative Procedures*

Operation	Total Number of Operations	Mortality		
		Early	Late	Total
Ileostomy	12	6	4	10 (83%)
Colostomy	7	2	0	2 (29%)
Ileosigmoidostomy	1	0	0	0
Appendicostomy or cecostomy	19	2	2	4 (21%)
Colectomy	2	0	0	0
Total	41*	10	6	16

\* On 35 patients

two and one-third years. These patients died at home, and the cause of death is therefore not certain. Two of the deaths were probably due to a continuation of the colitis with possibly some intercurrent infection. Two deaths occurred as a result of operations performed in other hospitals at which time the ileostomies were taken down and the continuity of the bowel restored. One patient died of pneumonia and diabetic coma. In another patient a thrombosis of the arteries to both legs developed and death followed extension of the thrombus up the lower part of the aorta. As is shown in table 1, the largest percentage of deaths occurred in the acute cases.

Table 2 presents figures for the mortality associated with the various types of operative procedures used. The most startling figure is that for the ileostomy group which shows a mortality of 83 per cent. It is also somewhat surprising to note that appendicostomy and cecostomy, generally considered the most conservative of all surgical procedures, carried a mortality of 21 per cent.

The tumor, which was on the right side, was extremely small (fig 11) It originated in the region of the isthmus of Scarpa's ganglion and histologically (fig 12) was very similar to the growths in the preceding cases. An abnormal network of blood vessels was seen in the vicinity of the tumor.

This was the smallest acoustic tumor we have seen. It originated in the vestibular division of the eighth nerve.

CASE 5—A Negro aged 37 died in January 1931 at the Baltimore City Hospital (Bay View) of pulmonary tuberculosis. The audiometer test, made three weeks

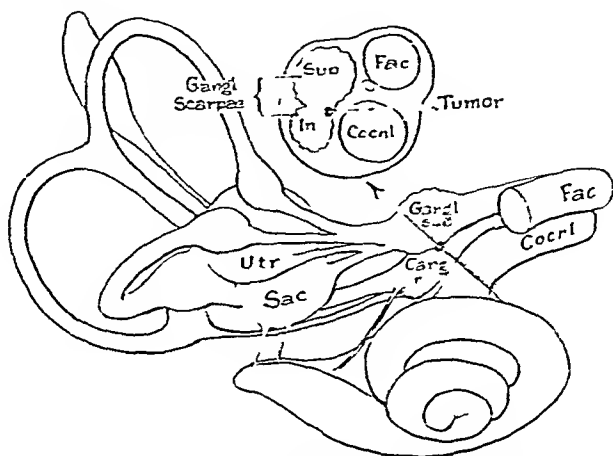


Fig 11 (case 4)—This was the smallest tumor of the group, it lay entirely within Scarpa's ganglion.



Fig 12 (case 4)—This section shows the tumor at its greatest diameter (0.25 mm), with normal nerve fibers and ganglion cells of the vestibular nerve,  $\times 130$ .

before death, showed normal hearing for low tones and some impairment bilaterally for the frequencies above 256 double vibrations. There was no history of tinnitus or of vertigo. The patient was quite ill. Spontaneous nystagmus was not noted. The caloric vestibular test caused normal reactions on the right but a retarded and very feeble nystagmus on the left side.

The tumor differed from those described previously in that it was bilateral and involved the cochlear rather than the vestibular division of the acoustic

improve following operation were treated by the irrigation type of therapy. It is also noteworthy that two of the three patients who were called "clinically well" have had colectomies.

#### CASE STUDIES

As might be inferred from the foregoing tables and the comment, there has been a tendency in this clinic during the past four years to treat more of the patients by the irrigation technic, using either an appendicostomy or a cecostomy for this purpose. This trend has been brought about not only by the higher mortality connected with the more radical procedures but by the distressing conditions that we have seen as a result of ileostomy. It has not been uncommon in our experience to have a patient tell us that he would rather be dead than go on living with the opening into the ileum, we have had to admit in certain cases that the patient was probably justified in such a statement. It is chiefly for this reason that we have returned to a more conservative form of therapy, and at this time report a series of eighteen cases in which colitis was treated in this way. We have analyzed this group of cases rather closely to determine, if possible, whether or not such temporization was justified. The few facts that we have learned can be brought out best by a few isolated illustrative case studies.

*CASE 1*—A 22 year old man entered the hospital with very advanced ulcerative colitis of two years' duration. He was having as many as twenty-four stools daily, containing blood and pus. He had lost 30 pounds (13.6 Kg.) and showed all the signs of depletion. An appendicostomy was done, following which the course was stormy. Irrigations were carried out but seemed to aggravate rather than improve the condition. After a trial of this therapy for about five weeks without much improvement, an ileostomy was done. This was followed by marked improvement with gain in weight and strength. He continued to bleed, however, and his anemia kept him constantly under par. For this reason he was subjected to a total colectomy, which was done in two stages. He is now clinically well, and the ileostomy opening is functioning satisfactorily.

This case is reported as an example of an appendicostomy which failed to bring about improvement. Briefly it represents a conservative measure being applied to a very advanced lesion.

*CASE 2*—A 23 year old woman entered the hospital with advanced ulcerative colitis of two years' duration. She was having from twelve to eighteen stools daily, containing blood and pus. She was going down hill rather rapidly, had lost 40 pounds (18.31 Kg.) and was very anemic. An appendicostomy was done, and under irrigation therapy she made definite improvement to a certain level then improvement stopped. She continued to bleed from the rectum, and her anemia held her down. One year later a colostomy was done in the mid-transverse colon, a roentgenogram having previously shown the bowel proximal to this point to be comparatively normal.

The colostomy was followed in three months by the first stage of a colectomy, at which time the rectum and lower portion of the sigmoid were removed by an

The tumor was on the right side. As shown in figure 14, the growth did not invade but pushed aside the cochlear nerve. The growth was traced from the internal meatus through an opening in the cribriform plate to a nodular expansion above the group of cochlear ganglion cells supplying the upper basal coil. The nerve structures in this region also were not destroyed but were pushed aside. Figure 15 shows that the tumor contained glial tissue and nerve cells with marginal Nissl bodies.

The acoustic nerve on the left side was pulled out at autopsy, so we do not know whether or not a similar growth was present in the internal auditory canal on this side. There was no tumor in the modiolus.

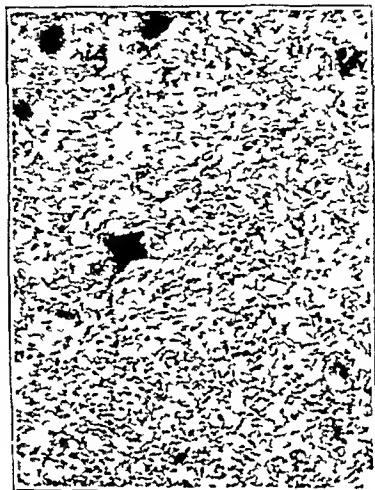


Fig 15 (case 6)—This is a section of a typical area of this unique tumor, which consisted of glial tissue with scattered nerve cells. A process of one of these cells is caught in the plane of the section,  $\times 130$ .

#### SUMMARY

Examination of serial sections of the temporal bones in two hundred and fifty cases revealed a small acoustic tumor in six. Each growth was entirely within the internal auditory canal. The largest was about 5 mm in diameter and the smallest about 0.25 mm.

The vestibular nerve was involved by four of the tumors and the cochlear nerve by two.

Histologically, five of these tumors were alike in cellular structure, they resembled large tumors found on the acoustic nerve and in the cerebellopontile angle. The sixth tumor was different from any growth we have seen in this locality.

An angiomatous network of blood vessels was present in three cases in which there were tumors and in seven of the other cases, the network involved the vestibular nerve.

These lesions, both the tumors and the angiomatous network, were asymptomatic. Irritative symptoms are not produced by growths that are too small to cause compression of the contents of the internal auditory canal.

marked sepsis and died twenty-four days after operation. Autopsy revealed generalized peritonitis (fig 2)

This represents a type of case in which the irrigation type of therapy seems definitely contraindicated. It is difficult to avoid the conclusion that the irrigations stirred up the bleeding and infectious process. It appears that the patient required some operative procedure to side-track the fecal stream and put the diseased bowel at rest. It is probably this type of case that is responsible for the often used phrase "ileostomy to save life."

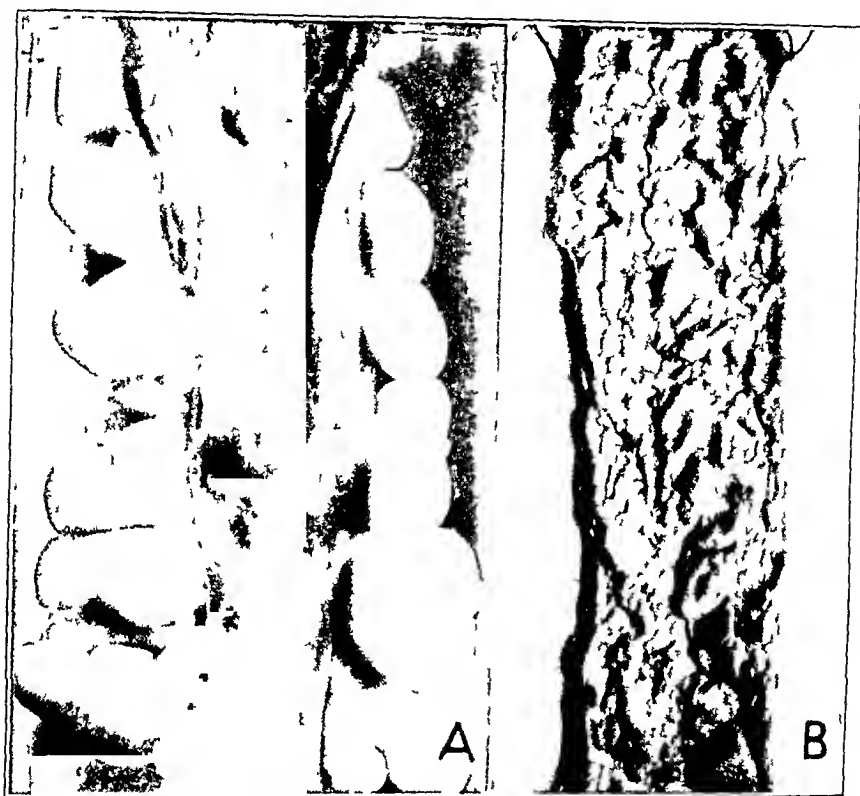


Fig 2—*A*, photograph of a portion of the colon from case 2 (W M). This shows the complete loss of haustrations—the garden hose type of colon. Several polyps are present. The great accumulation of fat outside the bowel is also quite characteristic (surgical specimen).

*B*, photograph of the colon (autopsy specimen) from case 3 (M S). This shows an entirely different picture with ulceration and polypoid hyperplasia. This case was marked by a great deal of blood in the stools.

**CASE 4**—A 26 year old man entered the hospital complaining that he had had bloody stools, from ten to fifteen daily, for a month. He was febrile, was losing weight rapidly and was bedfast because of weakness. A cecostomy was done, and irrigations were carried out. His postoperative course was very stormy and he gained slowly. After two months he was discharged from the hospital still averaging from nine to twelve stools daily, containing blood, and he had a daily tem-

## VITAL STATISTICS

We now may review a series of thirty-five cases of ulcerative colitis in each of which some operative procedure was done as a direct attack on the colitis. The cases were proved by proctoscopic and roentgenologic examination to be of the true "idiopathic" type. The vital statistics of the entire group are as follows.

There were fourteen males and twenty-one females. All were white with the exception of one colored female. The average age at the time of operation was 30 years, the youngest patient being 5½ years old and the oldest 58 years. Most of the patients had been admitted to the hospital on previous occasions, the number of admissions ranging from none to six, the average being one. During recent years there has been a tendency to operate sooner, and the medical department is apt to refer the patient to the surgeons at once rather than to give prolonged trial to a medical regimen. The average duration of the disease at the time

TABLE 1—*Mortality Classified as to Phase of Disease Treated by Operation*

Group	Total Number	Patients Dead			Patients Living
		Early	Late	Total	
1 Patients operated on during an acute phase of the disease	12	6	3	9 (75%)	3 (25%)
2 Patients operated on during a chronic phase of the disease	23	4	3	7 (30.4%)	16 (69.6%)
Total	35	10	6	16 (46%)	19 (54%)

of operation was three and one-fourth years, the longest duration being fifteen years and the shortest one month. Forty-one operative procedures were performed on the thirty-five patients, several patients had two or three operations. These forty-one operative procedures included twelve ileostomies, seven colostomies, one ileosigmoidostomy, six cecostomies, thirteen appendicostomies and two colectomies. There were also five plastic operations for prolapse, herniation, fecal fistulas, etc.

Table 1 shows the patients classified according to the clinical picture presented at the time of operation. About a third of them were operated on during an acute phase of the disease. Three of these were seen during their first fulminating attack, the others were seen during an acute exacerbation of a chronic process. Four patients had associated acute complications which included perianal and perirectal abscesses, intestinal obstruction, acute infectious arthritis and otitis media. Four patients had a chronic type of complication, such as stricture, fistula in ano and rectovaginal fistula.

## MORTALITY

The patients who died have been divided into early and late groups depending on whether they died in the hospital as a result of operation

from six to ten stools daily, anemia and symptoms of depletion the lesser of the several evils offered her

CASE 6—A 47 year old woman entered the hospital with a typical story of ulcerative colitis of seven years' duration. She was having from eight to ten stools daily with some blood and mucus. An appendicostomy was done and irrigations were begun. She showed rather steady improvement for about a year and was able to maintain her level of improvement. Her tube then became plugged up, and six months went by before she returned to the clinic. During those six months she went steadily down hill and lost almost all that she had gained. A new tube was installed and the patient sent home to build herself up again. She returned recently, much improved by frequent irrigations but dissatisfied with the "tube life." A barium sulphate enema showed the proximal portion of the colon to be uninvolved, and a colostomy will be done. This will probably be followed by colectomy.

The case is included here because it shows what usually happens when irrigations are stopped in those patients who previously did well on irrigation therapy. It emphasizes the point that the irrigation treatment is usually a permanent feature which the patient must be prepared to accept for life.

CASE 7—A 21 year old woman entered the hospital after three years of typical ulcerative colitis. She was having ten to twenty stools daily, containing blood and pus, and her lesions were extensive. A cecostomy was done, and after a stormy course she began to show slow improvement. Fourteen months have now passed and she is still faithfully irrigating every day. When she misses a day she has cramps and other abdominal discomfort. She passes very little blood, and her hemoglobin is only moderately depressed. During the first eight months she gained 20 pounds (9.1 Kg.) since then she has been able to maintain this level of improvement. Her colon roentgenographic series also shows rather marked improvement. The tube gives her little trouble and she is satisfied. She states that she would rather have the tube for life than endure a colostomy.

This case is included here because it probably represents about the maximum which can be promised a patient with the irrigation type of treatment. The next case is probably the exception to the rule and is the one case in which a patient treated by this method has been placed in the "clinically well" column.

CASE 8—A 49 year old farmer was seen with a typical history of ulcerative colitis of one year's duration. His symptoms were classic, with diarrhea, blood, mucus and pus in the stools, fever, and loss of weight. An appendicostomy was done and irrigations were started. Improvement was immediate and seemed permanent, so he stopped irrigating. When last seen he had been symptom-free for eighteen months. During this time the tube had been left in his side but was functionless. He was having one or two formed stools daily without blood, pus or mucus, was afebrile, ate a general diet, and felt well and strong. He was doing heavy farm labor. A barium sulphate enema showed no improvement whatever in the appearance of the colitis. However he was willing to gamble on a return of the disease, so with some misgivings the tube was removed. We have heard from him since and he is still clinically well.

## STATUS OF LIVING PATIENTS

There are nineteen patients, or 54 per cent of our series, who are living, and we were able to make follow-up examinations or to obtain reports on all of these. Classified as to type of disease (table 3), most of them fall into the group with chronic colitis. On the basis of their present status they have been classified in four groups: (1) those who failed to improve and are now the same or worse than they were before

TABLE 3—*Status of Living Patients Classified as to Phase of Disease Treated by Operation*

Group	Total Number	Patients Dead	Status of Living Patients			
			Not Improved or Worse	Improved But Improvement Now Stationary	Still Improving	Clinically Well
1 Patients operated on during an acute phase of disease	12	9	0	1	1	1
2 Patients operated on during a chronic phase of disease	23	7	3	9	2	2
Total	35	16 (46%)	3 (8.6%)	10 (28.5%)	3 (8.5%)	3 (8.5%)

TABLE 4—*Status of Living Patients Classified as to Operative Procedures\**

Operation	Number of Operations	Status of Living Patients				Total Living
		Not Improved or Worse	Improved But Improvement Now Stationary	Still Improving	Clinically Well	
Ileostomy	10	0	0	0	0	0
Colostomy	6	0	4	0	0	4
Ileosigmoidostomy	1	0	1	0	0	1
Appendicostomy or cecostomy	16	3	5	3	1	12
Colectomy	2	0	0	0	2	2
Total	35	3	10	3	3	19 (54%)

\* Classified according to last operation performed

operation, (2) those who improved to a certain level following operation but in whom the improvement has now ceased, (3) those who are still improving, and (4) those who are clinically well. The patients in the last group are symptom-free and show definite evidence of the permanency of this state.

Table 4 shows these results according to the type of operative procedure used. Several of the patients have had more than one operation and are therefore classified according to the last procedure carried out. It is interesting to note that all three of those patients who failed to



all tried irrigation therapy for two or more years and are now in a stationary condition with the disease still active enough to prevent them from becoming useful citizens

With the foregoing information at hand we have been forced to draw certain conclusions concerning the surgical treatment of ulcerative colitis in general. When each operative procedure is considered separately what has each to offer and what factors contraindicate its use?

#### ILEOSTOMY

Ileostomy is still the choice of the surgical profession at large in the treatment of this disease. Its disadvantages are well known. The fecal discharge is profuse, watery and irritating. Dehydration and inanition are difficult to control, and true vitamin deficiency diseases may result. In addition the operation carries with it a rather menacing mortality.

It is true that in many cases a physiologic adjustment occurs by virtue of which the discharge becomes less fluid, and some patients may even acquire habits whereby there are only two or three stools through the ileostomy every twenty-four hours. However, we know of no way to predict in advance which patients will be able to make this physiologic adjustment and which will not. It may be said in this connection that we have better functioning ileostomies since we have been employing the single-barreled technic, the blind distal loop being dropped back into the abdomen. Up until six years ago we commonly made a double-barreled type of ileostomy with the vain hope of later reuniting the ends of the bowel.

Some patients are so miserable as a result of their ileostomy that the surgeon is ever listening to their pleas to reestablish the continuity of the bowel regardless of whether the symptoms of the colitis return or not. We have heard patients state that they would rather die than endure an ileostomy, and there are probably a few cases in which the patient must make just such a decision. The experience of the past indicates that in the acute fulminating cases with progressive failure there is nothing short of ileostomy that will save life.

In the chronic cases the roentgenogram will occasionally show that the disease process stops short of the ileocecal valve, and that the cecum, ascending colon and occasionally part of the transverse colon are not involved. Such cases are in the minority, however, and in our experience this has been true in only about 25 per cent of the series. As a rule the process begins in the rectum or sigmoid and spreads proximally, and the earlier one sees a case the more likely is one to find an uninvolved portion of proximal colon. It is important to bear in mind this so-called regional type of ulcerative colitis which has been emphasized

abdominal perineal approach. The distal end of the blind loop of descending colon was brought out through the abdominal wall. Five months later the second stage was done, with removal of the blind segment of descending colon. She is now clinically well, all wounds have healed, and the colostomy has produced satisfactory functioning (fig. 1).

This case, like the first, makes clear that in cases of this severity appendicostomy and cecostomy are totally inadequate and that even ileostomy and colostomy may fail to arrest the disease. However, there was marked improvement following the appendicostomy, and the case illustrates how this simple procedure may be valuable as a first step by virtue of which the patient becomes a better risk for more radical surgical intervention. Colectomy was resorted to in both cases as a last resort.

CASE 3—A 22 year old woman entered the hospital with symptoms of ulcerative colitis of two years' duration. She was having only two or three stools daily.

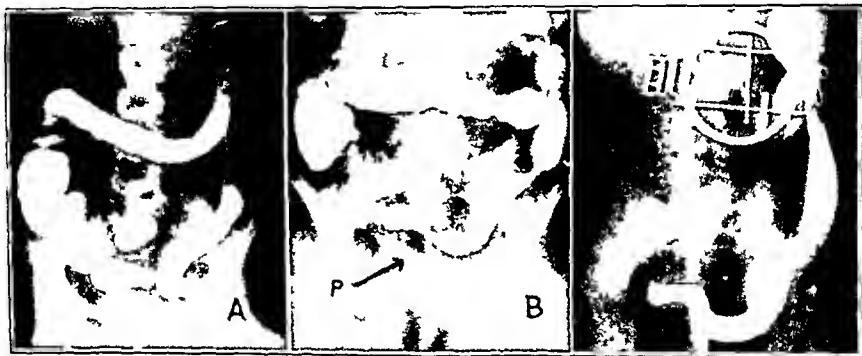


Fig. 1—A, a barium sulphate enema visualizing the colon in case 2 (W. M.) before surgical treatment, showing the rather typical garden-hose contour with loss of haustrations.

B, the same colon after fourteen months of irrigations through an appendicostomy tube. The irrigating tube is in place. The arrow indicates a few polypi in the lower portion of the sigmoid which could be seen by proctoscopy. Polypi are probably present in about 10 per cent of all cases of ulcerative colitis (Bargen and Comfort). The patient was markedly improved clinically but was still losing considerable blood by rectum. For this reason colostomy was done, in the mid-transverse colon.

C, the same colon several months after colostomy. There was still further improvement clinically, also some improvement shown in the roentgenogram. This patient later had a two stage colectomy with removal of the entire colon distal to the colostomy including the rectum. She is now clinically well.

but was losing much more than the usual amount of blood. At the time of operation she had fever and showed signs of toxicity. An appendicostomy was done and irrigations were started. The result was rather violent hemorrhages both through the tube and by rectum. She went from bad to worse, showing signs of

or undue fatigue is likely to cause a flare-up. It is therefore highly important to explain this to the patient *before* operation and impress him with the fact that the artificial anus must be accepted as a permanent affair. The literature is filled with reports of cases in which, after improvement has been made, the continuity of the bowel is restored, and the results are almost always disastrous. Either the procedure is marked by a fatality or the disease returns.

Knowing that the patients cannot be promised a cure, what can one promise them from ileostomy or colostomy? One can promise them definite clinical improvement. This improvement occurs and is often very striking. The extent of the improvement varies in different cases and probably depends for the most part on the extent of the lesions in the individual patient. Some patients improve to the extent that they are able to carry on their normal activities, and by watching their general health very carefully they are able to lead a fairly useful and happy life. This statement assumes that the ileostomy is functioning satisfactorily. Others never reach this level, the disease remaining active enough to keep them chronically anemic and in a state of semi-invalidism. It is this group of patients that brings one to the third operative procedure, namely colectomy.

#### COLECTOMY

Relatively speaking, colectomy is a new procedure in the treatment of ulcerative colitis. Ten years ago it was considered a very formidable procedure. Today it is rapidly gaining favor in all the leading clinics, not so much as a procedure of choice as a procedure of necessity. By doing this operation in several stages it has become possible to remove the entire portion of diseased colon in patients who obviously constitute poor surgical risks with a mortality which is little greater than that usually ascribed to major surgical operations on the large intestine for other conditions. On the whole the results have been very gratifying, and although there are as yet no clinics reporting five or ten year cures, there is every indication that the present good results will be permanent.

The two cases in which this treatment has been used in this clinic are quite recent, but their course to date has been very satisfactory.<sup>1</sup> This method of treatment has been used as a last resort, and justly so. It should probably always be a secondary operation. The indication

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1 Since this paper was written there have been five additional colectomies performed in this clinic for ulcerative colitis. Another colectomy was performed, which was not included in the foregoing series because of uncertain diagnosis; it is now felt that the patient falls into the group with idiopathic ulcerative colitis. This makes a total of one complete and six partial colectomies that have been performed in this clinic in the treatment of this disease. The usual method has been a two stage procedure and three of the cases are still awaiting the last stage. There have been no deaths.

perature of about 100 F. Two months later he went to another institution and took a course of serum and vaccine treatments. He made temporary improvement, but soon after he returned home thrombosis of the vessels to the left leg and gangrene of that extremity developed. A few days later the right leg became similarly involved. Bilateral amputation was carried out. The postoperative course was stormy, and he died one week later. At autopsy there was complete occlusion of the arteries to both legs, the thrombus extending up the aorta as high as the renal arteries. One kidney was completely infarcted, the other partially so.

This case represents an attempt to treat by conservative measures a patient with acute colitis seen in a first fulminating attack. It seems that the irrigation type of therapy was definitely inadequate, and the indication was probably for ileostomy to save life.

CASE 5—An 18 year old girl entered the hospital with rather extensive lesions of two years' duration. She was having about fifteen stools daily with some blood. An ileostomy was done, which was followed by the most striking improvement we have ever witnessed in a patient with this disease. We felt that she had been veritably snatched from the grave. The transformation from an emaciated, dehydrated and desperately ill person to a well developed and nourished girl with good color and strength was little short of miraculous. However, she had a great deal of trouble, first with herniation and later with closure of the ileostomy opening, necessitating dilatation and plastic operations. After seven admissions to the hospital she was so miserable that the opening into the ileum was closed and an appendicostomy tube substituted. She did very well for a while but continued to have from six to eight stools daily and lost enough blood to keep her moderately anemic and under par all the time. There was considerable drainage about the tube and finally another plastic operation was necessary. This patient returned to the hospital recently in a state of complete discouragement. There was a profuse drainage from the appendicostomy wound which soiled her clothes in spite of massive dressings. She stated that she would be willing to endure the diarrhea if she could only get rid of the draining sinus.

Here is a case worthy of considerable thought. This girl knows what it means to have an ulcerative colitis untreated by surgical measures. She knows what it means to have an ileostomy, and although she admits that she felt better generally while she had the opening into the ileum than she ever has since she prefers to get along without it. She also knows what it means to have an appendicostomy, but she prefers to get along without it. It seems that we have here the living testimony of an intelligent patient against all forms of surgical treatment. If we were to insist on treating the colitis *per se*, the obvious thing to do would be another ileostomy followed by total colectomy. However, if we treat the patient herself, the procedure becomes somewhat debatable. With a certain degree of misgiving we finally complied with her wishes and closed the opening into her bowel. It seems highly probable that it may be necessary in the future to resort to radical surgical intervention. For the present, however she is content and considers having

of improvement, but his general condition remains stationary. He may become disgusted with the tube, which almost invariably has seepage about it with tender granulation tissue and a foul odor. If he stops irrigating or removes the tube he begins to lose ground.

It is true that some patients show rather striking improvement roentgenologically and proctoscopically, but usually the roentgenogram shows the colon continuing to narrow and foreshorten, with gradual assumption of the garden hose appearance. A cure comes rarely, if ever. The roentgenograms in figure 4 illustrate this point. It appears that the evidence of progress obtained by barium sulphate enema is not absolutely reliable, since we have seen definite clinical improvement occurring in patients while the roentgenogram revealed progressively



Fig 4—*A*, the colon of R. L. before surgical treatment for ulcerative colitis. The symptoms were moderately severe.

*B*, the same colon after six months of irrigations through an appendicostomy. The irrigation tube is in place. Still further foreshortening has taken place, and the caliber of the bowel is even more contracted. However, the patient has made marked improvement clinically and is still slowly improving. This shows the difficulty in differentiating roentgenographically between progression of the disease and healing.

increasing loss of haustrations, narrowing and foreshortening. The difficulty appears to be the inability to differentiate the roentgenologic picture of healing from that of progression of the disease. In this connection it has also been noted that the colon continues to contract and diminish in caliber after short-circuiting operations, such as ileostomy. Whether these changes are due to a continuation of the disease or whether they represent healing is a question which the roentgenolo-

## ANALYSIS OF THE APPENDICOSTOMY-CECOSTOMY GROUP

Of the entire group of eighteen patients treated by the irrigation method, four are dead. Two more have had subsequent colectomies, but it probably does not follow that they should be included as presenting failures of the method. In three more the tube either came out or was removed. All three showed clinical improvement as long as the tube was in place. One has been able to maintain this improvement since the tube came out, and his condition can be classed as improved but stationary. One went back to her original state after accidental removal of the tube and has been in that state ever since. The third is definitely worse than before—bedfast, bleeding and ill. This leaves eight patients who still have the tube in place and are irrigating faithfully. The length of time since operation varies from seven to twenty-six months, the average being fifteen and one-half months. To these patients must be added the one from whom I purposely removed the tube and have classified as clinically well.

The results in this group of eighteen patients are as follows:

Dead	4
Treatment not followed (tube out)	3
Tube removed purposely patient clinically well	1
Subsequent colectomies patients clinically well	2
Tubes in place patients still irrigating	
Unimproved or worse	1
Improved but improvement now stationary	4
Still improving	3
Total	<hr/> 18

This seems to indicate that at least half the patients improve to a certain level and thereafter remain stationary. All three of those who are classified as "still improving" have had their tubes less than the average length of time for the group (seven, eight and nine months, respectively). It seems that one must wait at least a year before one can be sure that the maximum benefit from the procedure has been obtained. On the law of averages it seems likely that those three patients will in a few more months fall into the stationary group rather than the clinically well group.

In analyzing the personal reactions of the patients it was interesting to find that only two of the eight patients now having tubes were badly dissatisfied with their results. The other six patients were anxious to get rid of the tube and were more or less discouraged but on the whole were fairly well satisfied with their improvement.

Of the eight patients probably at least three are now candidates for more radical surgical intervention, i. e. colectomy preceded by either ileostomy or colostomy. This opinion is based on the fact that they have

The following classification is based on both the clinical symptoms and the pathologic process as shown by barium sulphate enema

- 1 Acute fulminating cases
- 2 Severe chronic cases
  - A Roentgenogram shows the entire colon involved
  - B Roentgenogram shows only a portion of the colon involved (regional form)
- 3 Mild cases

Group 1 represents cases of the disease in an acute phase with fever and many liquid stools containing much blood, the patients presenting a picture of rapid progressive failure due to depletion and anemia. We feel that the indication for surgical treatment in this group is definite. There is no longer any need for procrastination. The treatment of choice is probably to side-track the fecal stream at once by ileostomy or colostomy, by the latter when the pathologic process is of the regional type.

Group 2 includes the chronic cases with advanced pathologic change and is by far the largest group. There is usually a history of failure to improve following medical therapy. In these cases there is more time to deliberate. The roentgenograms should be studied carefully as to the extent of the disease, because the treatment differs on the basis of these findings. On the strength of the roentgenologic findings this group is divided into two subgroups. Most of the cases will fall into subgroup A, and one is then obliged to offer the patient either ileostomy or the irrigation type of therapy. The advantages and disadvantages of each have been discussed. Which procedure to recommend depends for the most part on the severity of the lesions and the type of person with whom one deals. If the condition is far advanced and it is felt that a colectomy will eventually be necessary, it may be better to advise ileostomy, which will serve as the first step toward that procedure. Appendicostomy or cecostomy is the alternative, and the decision as to the wisest procedure depends largely on the merits of the individual case. We feel quite definitely in this clinic that the mortality figures can be lessened by doing more appendicostomies as a preliminary step to ileostomies.

A few cases in group 2 will fall into subgroup B. The treatment of choice in these cases seems to be colostomy. In all the cases of groups 1 and 2 the possibility of an ultimate colectomy should be kept in mind.

Group 3 includes cases in which the disease is mild and in which a decision has to be made between medical and surgical treatment. The irrigation type of therapy offers a convenient compromise for these patients.

in the literature of the past few years (fig 3) Knowing what we do about ileostomies, it would seem most unfortunate to subject a patient to an ileostomy when a colostomy would serve the purpose

It appears, therefore, that there are two main indications for ileostomy The first is in the acute fulminating cases with progressive failure in which it is probably a life-saving measure The second is in the most severe chronic cases with advanced lesions involving the entire colon

#### COLOSTOMY

The purpose of colostomy is the same as that of ileostomy—to divert the fecal stream and put the diseased colon at rest Colostomy, however, offers a condition much more compatible with a normal exist-



Fig 3—4, the colon in case 5 (E L), showing a rather marked degree of ulcerative colitis involving the entire colon The patient had had an ileostomy opening two years at the time this picture was taken

B, the colon of J B, exemplifying regional ulcerative colitis The disease is limited almost entirely to the transverse colon, and the other portions of the bowel are uninvolved

tence There is no great nutritional problem A preoperative barium sulphate enema is necessary to determine the extent of the disease The patient who has some normal proximal colon through which to make a colostomy is indeed fortunate

Prognosis concerning the results of either ileostomy or colostomy must always be guarded A cure cannot be promised The disease persists and can be seen by proctoscopic examination There may be marked clinical improvement but the disease process is still there in a latent form and any slight infection of the upper respiratory tract exposure



## DUPUYTREN'S CONTRACTURE

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The French surgeon Dupuytren in 1832 described a flexion deformity of the fingers caused by thickening and shortening of the palmar fascia. The gradual onset of this deformity, with little or no pain, is characterized by the formation of a firm, fixed nodule in the palmar fascia at the linea mensalis, usually near the base of the ring finger. In time the nodule involves the entire palmar fascia, including the attachments to the sides of the fingers, and contracture of the palm and fingers is produced (fig 1). The skin becomes involved early, it presents a dry, wrinkled, hard and often calloused appearance and is adherent to the hypertrophied fascia. The subcutaneous fat is lost, but the tendons are not involved. The cordlike contracture of the palmar fascia is brought into a tense position when an attempt is made to extend the finger or fingers, and this is often mistaken for evidence of contracture of the tendon. The deformity is usually bilateral, commonly it begins in the right hand, and months or years later the left hand will become involved. As the palm and fingers become more flexed, loss of power to open the hand causes disability, this increases with time until the patient is confronted with loss of function of the hands. This is a calamity to a skilled workman and threatens his future earning capacity. He therefore consults a physician for relief. Fortunately, in most cases, modern aseptic surgical technic permits correction of the deformity caused by Dupuytren's contracture and return of good function of the hand.

A disease that produces a disability which affects the patient's earning capacity may assume economic and medicolegal importance, and then the etiologic factors, such as trauma, infection and heredity, become important. In this age of insurance, workmen's compensation and employers' liability, patients are likely to ascribe their disability to irritation resulting from their occupation, to a bruise, cut or infection. As long as the disease is unilateral and there has been an unquestioned local injury, those concerned appear to associate the two as cause and effect but with the appearance of a similar lesion in the other hand the condition is not so readily explained. Focal infection and general dis-

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From the Section on Orthopedic Surgery, the Mayo Clinic

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for it is fairly clear—it is reserved for those cases in which a satisfactory level of improvement has failed to be obtained after one of the less radical procedures. It should not be resorted to until the patient has had at least a year's trial of ileostomy or colostomy. Some clinics prefer to wait from two to three years. Our experience has shown that very little improvement can be expected after the first year.

#### ILEOSIGMOIDOSTOMY

This is a method of treatment based on the principle of putting the diseased bowel at rest by shunting the fecal stream around it. In principle it is sound, but it is seldom applicable for the simple reason that the sigmoid colon is practically always involved in the disease. There is, however, an occasional case of regional colitis in which the procedure may be applied with benefit.

#### APPENDICOSTOMY OR CECOSTOMY WITH IRRIGATION THERAPY

It is with this type of therapy that this paper is most concerned. What does it offer the patient with ulcerative colitis? What are its contraindications? We have found that the typical course following this type of therapy is one of immediate improvement which is usually too encouraging, since it does not accurately portray the end-result.

The procedure is simple and can be done through a short muscle-splitting incision. The appendix is freed and the meso-appendix ligated in the usual manner for appendectomy. Amputation of the appendix is then carried out, leaving a short stump (from 1 to 2 cm.) through which a small catheter is threaded into the cecal lumen. We usually employ a no. 12 or no. 14 French catheter. The stump is then inverted by means of a purse-string suture. If the appendix is absent or extensively bound down by adhesions, the catheter is introduced directly into the cecum and held in place by a purse-string suture. The operation can be done quickly, and the patient suffers little general reaction. After a few days irrigations are begun through the tube by the usual gravity method. We formerly used a hypertonic saline solution (from 1.25 to 2 per cent) on the theory that the element of dehydration of the edematous bowel might be of benefit. However, we found that about half the patients were unable to tolerate the hypertonic solution because of increased cramps and abdominal discomfort. After going home most of them will not bother to make up an accurate solution but will resort to plain water with perhaps a teaspoonful of salt to the pint for irrigation purposes. We have not been able to find any relation between the type of irrigating fluid used and the result obtained.

After a period of about a year the improvement usually stops. If the patient continues to irrigate he is usually able to maintain this level

nature of the contracture is not commonly recognized and that the benefits of modern aseptic surgery are not generally appreciated. In too many instances a surgeon is not consulted until extension of the contracture has involved several fingers (fig 2) and the finger-tips are invaded with extensive involvement of the skin, peripheral nerves and blood vessels. The contracted and thickened fascia should be excised early to obtain the best results.

It is generally conceded that the condition afflicts more males than females. In my series 241 patients, or 88 per cent, were males, and 32 or 12 per cent, were females. The average age of these patients was 54 years, the youngest patient was 17 and the oldest 80 years of age. Of the 273 patients affected with Dupuytren's contracture, 175, or 64 per cent, had involvement of both hands, the right hand only was

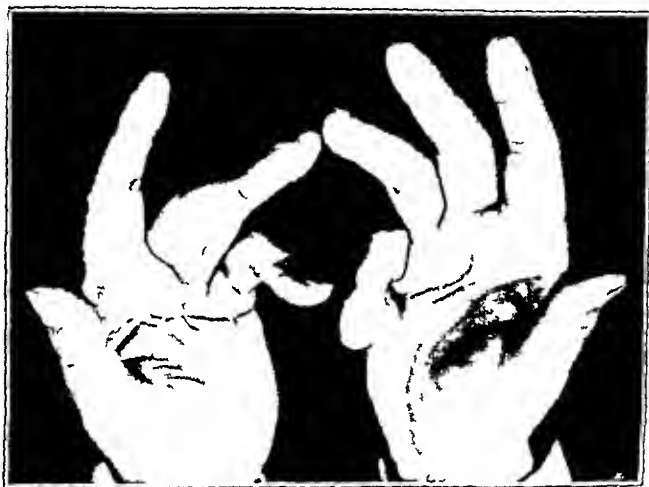


Fig 2—Dupuytren's contracture of grade 3

involved in 69 cases, or 25 per cent, the left hand only was involved in 29 cases, or 11 per cent. Thus, of the 98 patients with unilateral involvement, the right hand was affected in 70 per cent. The duration of the involvement varied from several weeks to twenty-five years.

Laborers, including farmers and mechanics, and others who work out of doors or whose hands are subjected to stress numbered 123, or 45 per cent, and mental workers and those whose hands are not subjected to stress, 150, or 55 per cent. The occupations of the 273 persons are given in table 2. Although the type of occupation given at the time of examination often indicated that the patient led a sedentary life, many bankers, school teachers and physicians had been accustomed to doing the most strenuous kinds of labor earlier in life. Of the 273 patients whose condition was diagnosed as Dupuytren's contracture 84, or 31 per cent, were subjected to operation.

gist cannot always answer. We should prefer, therefore, to base our conclusions concerning progress on the clinical course and proctoscopic findings.

Most clinics in which ulcerative colitis is treated have no place in their program for the irrigation type of treatment. However, we are convinced in this clinic that it has a place, and we feel that those clinics are ignoring a method of treatment which is of considerable help in selected cases. We prefer to think of the irrigation type of therapy as a compromise between straight medical management and ileostomy. In this rôle it offers the patient with mild chronic colitis a chance of improvement to a level compatible with normal living. In the more severe chronic colitis it offers both the surgeon and the patient an alternative to ileostomy. Whether it should be considered when colectomy is possible is a more debatable problem. But when the procedure at stake is ileostomy with its obvious disadvantages, one is able to offer the patient an alternative with some merit. We feel that appendicostomy or cecostomy may yield the patient with moderately severe chronic colitis an improvement fully as striking as that seen after ileostomy, and with much less risk. The patient must not expect a cure, and he must be prepared to accept the tube as a permanent handicap. Every few months the tube must be changed. He must also be willing to face the possibility that more radical surgical intervention may eventually be necessary or advisable. Lastly, we have found that appendicostomy or cecostomy is of value as the first step toward a more radical surgical procedure, such as colectomy. The operation enables the patient to improve and become a better surgical risk for the subsequent ileostomy or colectomy.

On the other hand, we have learned certain rather definite contraindications to this form of therapy. It is contraindicated when the disease is in an acute phase with many stools containing much blood and with high fever. Irrigations then may provoke further bleeding and only stir up the process. Another factor worthy of consideration is the intelligence of the patient and his ability to cooperate. The success of the treatment depends in such large part on the cooperation of the patient in carrying out the irrigations that the method is definitely contraindicated in certain cases on this ground alone.

#### PROGRAM OF TREATMENT

In the light of our present knowledge, and using the foregoing line of reasoning, we have attempted in this clinic to formulate a more definite program for the treatment of ulcerative colitis. In the first place it seems useful to have some method of classification of cases which in itself will point the way toward more intelligent treatment.

operated on at the clinic. The patients were questioned regarding the relationship of injury to each hand, with the following results. A positive history of injury was obtained concerning 35 hands and a history of infection concerning 5 hands, the histories were uncertain concerning 16 hands, and there was no history of injury concerning 81 hands. Thus there was a positive history of trauma to 25 per cent of these 137 hands and a history of infection of 3.6 per cent.

In reviewing the complaints made at the time of examination I found that 45 per cent of the patients gave histories of deformity, contracture or aching, and some said that at times there was a puckling sensation in the palm of the hand. There was a history of deformity and pain in the hands or feet in 125 cases, or 46 per cent of the total of 273 cases, of gastro-intestinal symptoms in 38, or 14 per cent, and of rheumatism in 22, or 8 per cent. There were neurologic factors in 18, or 6 per cent, genito-urinary symptoms in 12, or 4 per cent, backache in 10 or 3 per cent, malignant disease in 6, or 2 per cent, cardiac symptoms in 6 or 2 per cent, headache in 6 or 2 per cent, syphilis in 6, or 2 per cent, hernia in 4, or 1 per cent, flat feet in 3, or 1 per cent, disease of the skin in 2, or 1 per cent, goiter in 1, or 0.3 per cent, diabetes in 1 or 0.3 per cent, and pulmonary symptoms in 1, or 0.3 per cent. In 12 cases or 4 per cent, in which there was no history relative to the hands the contracture was discovered in the course of routine physical examination.

The variety of complaints and the findings at the time of examination did not seem to place any one condition or disease as having established a relationship of sufficient importance to be considered outstanding, in my opinion. The etiology, to which reference was made earlier in this paper, is still obscure. Authors have reported Dupuytren's contracture in association with arteriosclerosis, multiple sclerosis and syringomyelia but I believe that such association is merely coincidental. The dependability of the theory that the condition is neurologic also remains undetermined. Repeated injuries to the ulnar nerve and local injuries in the region of the eighth cervical and first thoracic vertebrae, with possible irritation of the sympathetic ganglions, trophoneurotic manifestations have been considered. When one reviews the records of the patients it is difficult to be satisfied with the theories. I believe that the hereditary factor is of some importance, as I have already stated, and that the history, if carefully taken, will bring this out.

In discussing the degree of deformity, the following system may be utilized (table 4). 0 indicates that there is no deformity other than unnatural thickening of the palmar fascia and wrinkling of the skin and that there is no contracture of a finger, 1 indicates, in addition to the preceding conditions, definite contracture of one finger, but not more than 60 degrees of flexion in any one joint (the hand can grasp but

## SUMMARY AND CONCLUSIONS

A series of thirty-five cases of chronic ulcerative colitis has been surveyed to evaluate, if possible, the relative merits of the various operative procedures used

At this clinic we have found appendicostomy and cecostomy with subsequent irrigation of the diseased bowel a useful procedure in selected cases. The benefits to be expected from this procedure have been discussed on the basis of a series of eighteen cases in which this treatment was applied

A few general conclusions have also been expressed concerning the more radical types of surgical intervention

This study has emphasized again the limitations of all forms of surgical treatment and the apparent futility of expecting cures from any procedure less than colectomy

We feel quite definitely that any blanket form of therapy, i. e., one operative procedure used on all types of patients as they come, cannot give the best results. By carefully analyzing each case, by using certain procedures only in selected cases and by remembering certain limitations of each type of operation the present results can be improved to an appreciable degree

A simple classification of cases has been suggested which in itself points the way toward more intelligent treatment

This outline of treatment represents only a transient opinion rather than a permanent policy. There is no ideal method of treatment, and one is usually faced with the problem of choosing the least vicious of several evils. As experience increases new procedures may be developed which will make the present day methods seem entirely unsuitable. On the other hand, there may be new developments in the field of internal medicine which will thrust all forms of surgical treatment into obscurity. At the present time, however, surgery has something definite to offer these patients, and the problem involves the choosing from a number of procedures at one's disposal the one most suited to each case

and treatment postponed. Unfortunately, this often leads to extensive contracture and a poor prognosis, in spite of expert surgical treatment. Some patients came to the clinic following operations performed elsewhere, the results of which had not satisfied them. Thus, I had the opportunity to examine postoperatively 33 patients who had been operated on elsewhere. Six of these patients, or 18 per cent, seemed to me to have secured satisfactory results. In 22 of the 33 cases excision had been performed, with good results in 5, or 23 per cent, in 2 cases tenotomy had been performed, with failure in both instances, fasciotomy had been performed in 2 cases, with success in 1 and failure in 1, and in 7 cases amputation had been performed. In reviewing the records of these patients with postoperative Dupuytren's contracture it is obvious that lack of cooperation on the patients' part played an important rôle in the failure of the attempt to correct the deformity.

Subcutaneous fasciotomy may relieve the contracture in some of the lesser degrees of deformity, so long as great care is exercised not to injure blood vessels, nerves and tendons. However, treatment of Dupuytren's contracture is most successful when the contracted palmar fascia is removed and proper postoperative measures are applied. In order to accomplish this it is necessary to make an incision which will permit thorough exposure of the involved fascia. The longitudinal incision over the fourth metacarpal bone has been used most commonly in the past, but because of the difficulties of exposure and the tendency to irritation from repeated movement this method has been superseded by incisions made along the fifth metacarpal bone and transversely along the *linea mensalis* (a Z-shaped incision, fig 3A). Because the *linea mensalis* is formed as the result of flexion of the little, ring and middle fingers and because the palmar fascia (fig 3B) divides just distal to it and forms bands which pass to the fingers, incision at this point affords excellent exposure. Furthermore, the majority of contractures form in this area, at the base of the ring finger, and unless the fingers are involved by extension of the contracture it is seldom necessary to make a second incision in the palm. An anterolateral incision is used in dissecting out the fascia of the fingers (fig 4A). For some of the extensive lesions it is obvious that the skin must be sacrificed, because it is densely adherent to the hypertrophied fascia, in such instances the contracted skin and fascia are excised, and a skin graft of full thickness is applied to cover the defect. For many years I have used the cuff of the sphygmomanometer to obtain a bloodless field, releasing it occasionally to permit circulation and to facilitate isolation, and tying off of the small bleeding points with extra-fine catgut. It is highly important that the wound be dry and that the clots be removed before the wound is closed. Strong antiseptic substances should not be placed in the wound, and if any solution is used I prefer isotonic solution of sodium chloride. Great

ease, such as arthritis, may also be mentioned by the patient, or a family history may be volunteered. This history in every case should be carefully investigated as in some instances focal infection, trauma to the palm caused by repeated deep pressure and hereditary influences seem to be of importance.

The present study of material encountered at the Mayo Clinic is concerned with 448 hands of 273 patients afflicted with Dupuytren's

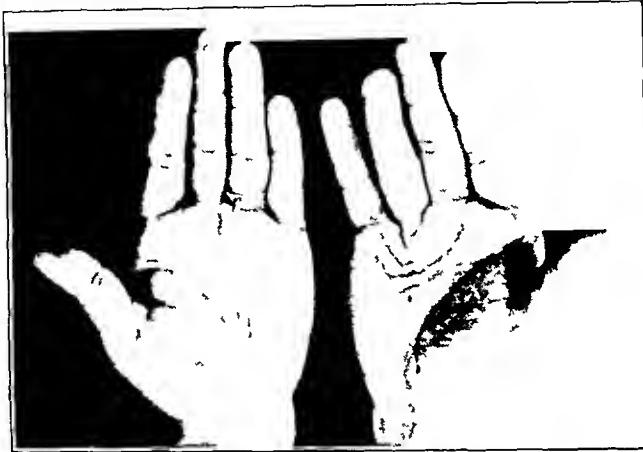


Fig. 1—Dupuytren's contracture in both hands, of grade 1 in the left hand and of grade 2 in the right.

TABLE 1—Fingers Involved in 448 Hands of 273 Patients

Fingers*	Unilateral Involvement	Bilateral Involvement	
		Right Hand	Left Hand
4	28	38	34
4 and 5	40	78	83
3, 4 and 5	7	22	12
3 and 4	3	6	4
5	12	18	21
1, 2, 3, 4 and 5	5	2	6
Foot and hand	3	7	11
	0	4	4
Total	98	175	175

\* Key to numbering of fingers: 1 thumb, 2 index finger, 3, middle finger, 4 ring finger, 5, little finger.

contracture (table 1). Many of the patients were greatly concerned over the impending disability, which threatened their livelihood, some had received advice that the tendons were involved and that surgical measures were of little or no value and might result in complete loss of function of the hands. Other patients came because of illnesses apparently not associated with the contracture and were resigned to the deformity as a part of senile change or as an incurable condition. My experience with these patients would make it apparent that the pathologic



care must be taken in handling the tissues, and fine hemostats and forceps, retractors with blunt edges and moist sponges are preferable.

I usually expose the narrow upper end of the palmar fascia, isolate it with small, blunt-pointed dissecting scissors, pass a hemostat under it and, after clamping it firmly, divide it with a knife (fig 4B). The fascia can then be raised by gently pulling the forceps away from the palm, and with a fine knife or scissors the fasciculi can be divided as they



Fig 5—*A*, tissue excised in a case of Dupuytren's contracture, *B*, lymphocytic infiltration of excised tissue

pass in the various directions. The dissection is continued distally until all contracted fascia has been freed, and should such fascia continue into the fingers separate incisions and dissections are made. At the time that the contracted fascia is removed (fig 5*A* and *B*) from the fingers, great care must be taken in separating the nerves and blood vessels from the fibrous mass in which they lie. Should the surgeon merely expose the fibrous mass and excise it, he may find later that the patient has resultant anesthesia and impaired circulation. I have mentioned the possibility

Foci of infection, which might be considered as possible etiologic factors, were noted in 141 cases, in the remaining 132 a definite focus was not noted on examination for discovery of one was not carried out. The tonsils and teeth were the most common sites of infection, 107 of the 141 patients, or 75 per cent, had infection of one or the other of those structures or of both. Of the 141 patients, 48, or 34 per cent, had dental infection alone, 18, or 12 per cent, tonsillar infection alone, and 41 or 29 per cent, both tonsillar and dental infection, foci of infection in other parts of the body, often associated with tonsillar or dental infection, made up the remaining 25 per cent. The incidence of known

TABLE 2—*Occupation of 273 Patients Who Had Dupuytren's Contracture*

Laborers carpenters, butchers, lumbermen and others whose hands are subjected to stress	67
Farmers	56
Merchants, bankers, managers	40
Clerks bartenders barbers telegraphers bookkeepers	31
Housewives	26
Physicians and dentists	19
Ministers	17
Teachers and students	10
Lawyers	7
Total	273

TABLE 3—*Foci of Infection Noted in 141 Cases of Dupuytren's Contracture*

Teeth only	48	Tonsils only	18
Teeth and tonsils	41	Tonsils and prostate gland	7
Teeth and nasal sinuses	2	Tonsils and nasal sinuses	2
Teeth and prostate gland	2	Prostate gland only	10
Teeth prostate gland and tonsils	2	Nasal sinuses only	4
Teeth and urethra	1		
Teeth tonsils and nasal sinuses	1		
Teeth and uterine cervix	1		
Teeth and gallbladder	1		
Teeth and skin (furuncle)	1		

focal infection was apparently high enough to be of some significance (table 3). Because many of these patients were examined in the years before attention was directed to focal infection the actual incidence of such infection may have been even higher than the figures given would indicate.

Trauma may be considered an etiologic factor, especially by those who possibly could benefit from workmen's compensation or insurance. Too much stress is often laid on some alleged or sustained injury to a hand which gives evidence of beginning contracture whereas inspection or an interval of time would bring out a bilateral lesion. I have reviewed the histories to find if possible whether trauma was a causative factor. Of the 84 patients on whom operation was performed 53 had bilateral involvement (20 of whom had only 1 hand operated on), and 31, unilateral involvement or of a total of 137 hands involved, 117 were

obtained by more conservative methods, but, of course, it has a limited field (fig 6)

I have operated on 117 hands of 84 patients, 13 of these hands had been operated on previously. Excision of the palmar fascia was performed on 97 hands, with excellent results in 55 cases, fair results in 11, and poor results in 8, the possessors of 23 of these hands have died or I have lost track of them. Six amputations were performed. Subcuta-

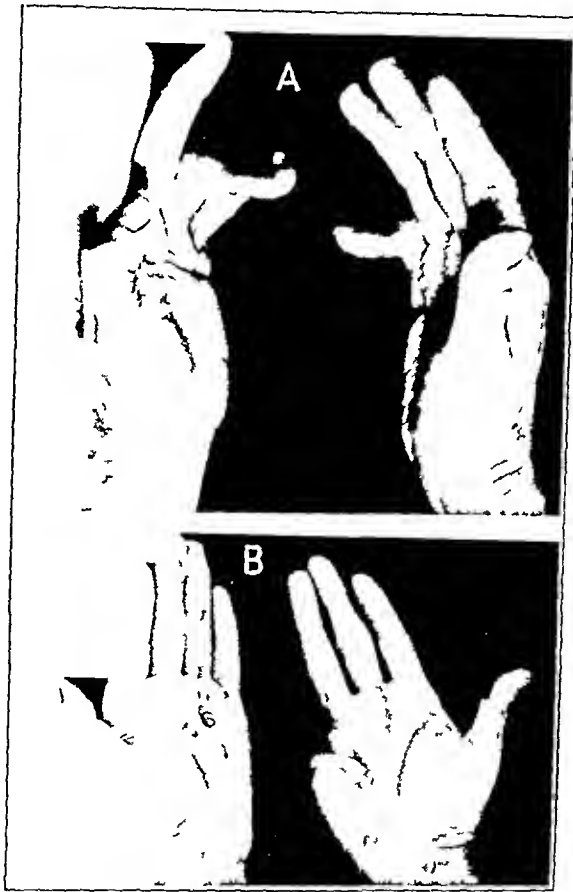


Fig 6—*A*, condition of the hands when the patient presented himself for treatment. The left hand had not been operated on, Dupuytren's contracture of grade 3 is evident. The right hand had been operated on, but Dupuytren's contracture of grade 3 is still evident, and ankylosis of the little finger is present. *B*, the same hands after primary operation on the left hand and secondary operation on the right. Skin and fascia were removed from the left hand, and the defect was filled in by a massive skin graft. The little finger of the right hand was disarticulated, and the skin of the finger was used as a pedicle graft.

neous fasciotomy was performed on 13 hands, with good results in 5 cases, fair results in 2 and failure in 2, I have lost track of the possessors of 4 of these 13 hands. One tenotomy is recorded as resulting in failure

there is not full extension of one finger), 2 indicates involvement of more than one finger, with definite contracture and inability to extend more than 60 degrees, 3 indicates contracture of two or more fingers and contracture of 90 degrees or more of one (the thumb and index finger may be opened and still be useful, although the hand as a whole cannot be opened for grasping), 4 indicates more or less contracture of all the digits, and the hand cannot be opened or the thumb fully extended (some of the articulations may be in acute flexion and ankylosed and a finger-tip may remain in contact with the palm)

In the presence of manual deformity, skilled workers, musicians, surgeons and others whose hands are subjected to stress have a higher

TABLE 4—*Deformity Noted in 259 Hands*

Grade	Right Hand	Left Hand
0	14	10
1	20	11
2	53	49
3	49	30
4	12	11
Total	148	111

TABLE 5—*Estimate of Occupational Disability Noted in a Study of 183 Hands*

Grade	Right Hand	Left Hand
0	22	27
1	21	10
2	33	32
3	20	11
4	1	1
Total	102	81

grade of occupational disability than have merchants, bankers, clergymen and others whose hands are not subjected to stress. The grade of occupational disability, therefore, may have little relation to the grade of deformity. The degree of occupational disability was not noted in the cases that form the basis of this report, but in reviewing the records I have attempted to estimate it and to grade it 0, 1, 2, 3 and 4. Thus, 0 would indicate practically no disability, or disability of from 0 to 10 per cent, 1 would indicate disability of from 10 to 20 per cent, 2 would indicate disability of from 20 to 40 per cent in a hand with involvement of one finger, 3 would indicate disability of from 40 to 60 per cent in a hand with involvement of two or more fingers, and 4 would indicate disability of from 60 to 100 per cent in a hand with contracture of all the digits and the palm (table 5).

It was often noted that although definite deformity was present the degree of disability and discomfort was minimized by elderly patients

The type of incision that Dr Meyerding mentioned, which extends along the distal flexion crease and proximad along the ulnar side of the hand and which can be supplemented by an anterolateral incision in the finger, is a very useful one, but other incisions are also of value, for instance one along the vertical crease of the palm in cases in which the contracture involves the central portion of the palm. In our work we have tried to adapt the incision to the individual case and at the same time to keep in mind the important principle that incisions should be made along flexion creases and not across them.

Finally, I should like to emphasize the last points that Dr Meyerding stressed: asepsis, careful preparation of the patient before operation, the use of a bloodless field, accurate hemostasis and, above all, atraumatism—handling the tissues with gentleness, not pinching them with forceps, and retracting them carefully, so securing for the patient the best possible result.

DR JOHN STACEY DAVIS, Baltimore (presented by DR G O EATON) If my memory is correct, Dr Meyerding's series of cases is the largest yet reported from any single clinic.

This disease of the palmar fascia is apparently a focal hypertrophy of the connective tissue originating in the walls of the smallest vessels and ending in contraction. The etiology is obscure, but I believe that one is justified in concluding that the fascial involvement is of idiopathic origin and is most apt to occur during middle age or in the senile period. So far as is known, there is no single constitutional or local disease with which Dupuytren's contraction is exclusively associated or of which it is a manifestation. In the majority of cases the condition does not appear to be specifically caused by trauma or local irritation, though these factors, as well as local or constitutional pathologic conditions, seem at times to have some exciting or contributing influence. There is no question, however, but that hereditary influence is shown in numerous instances. A comparison of some of the statistical tables given in Dr Meyerding's paper with those in a series of 40 cases reported several years ago by Dr Finesilver and myself shows them to be much the same.

Many methods of treatment have been advocated, but most of them are without merit. I have seen judiciously applied roentgen treatment apparently prevent the extension of the process and cause some softening in a few cases in which operative treatment was impracticable. I am convinced that the only method of treatment at one's disposal at present which can be depended on to cure the condition is excision of the palmar fascia, closure of the wound by sutures, the implantation of a whole thickness skin graft or a pedunculated flap, as indicated in the individual case, and long continued postoperative fixation.

DR A BRUCE GILL, Philadelphia I am convinced that in many cases Dupuytren's contracture is due to focal infection. Chronic fascitis resembles chronic myositis and chronic arthritis. I have observed cases of the acute type of Dupuytren's contracture in which there were redness, swelling, tenderness and local elevation of temperature. And I have seen these signs disappear on removal of focal infections. In other cases, which were without these acute manifestations but which were characterized by a steady, if slow, increase of the contracture, the condition became stationary after the same remedial measures. A dentist consulted me about eight years ago because of a steadily increasing contracture. I found that he had some badly infected teeth. He had them removed. The contracture ceased to progress, and he has never required operation.

I operated on a woman twelve years ago and removed the palmar fascia completely by the method which I reported in the *Annals of Surgery* in August 1919. Shortly after the operation all the joints of her fingers and hand became affected.

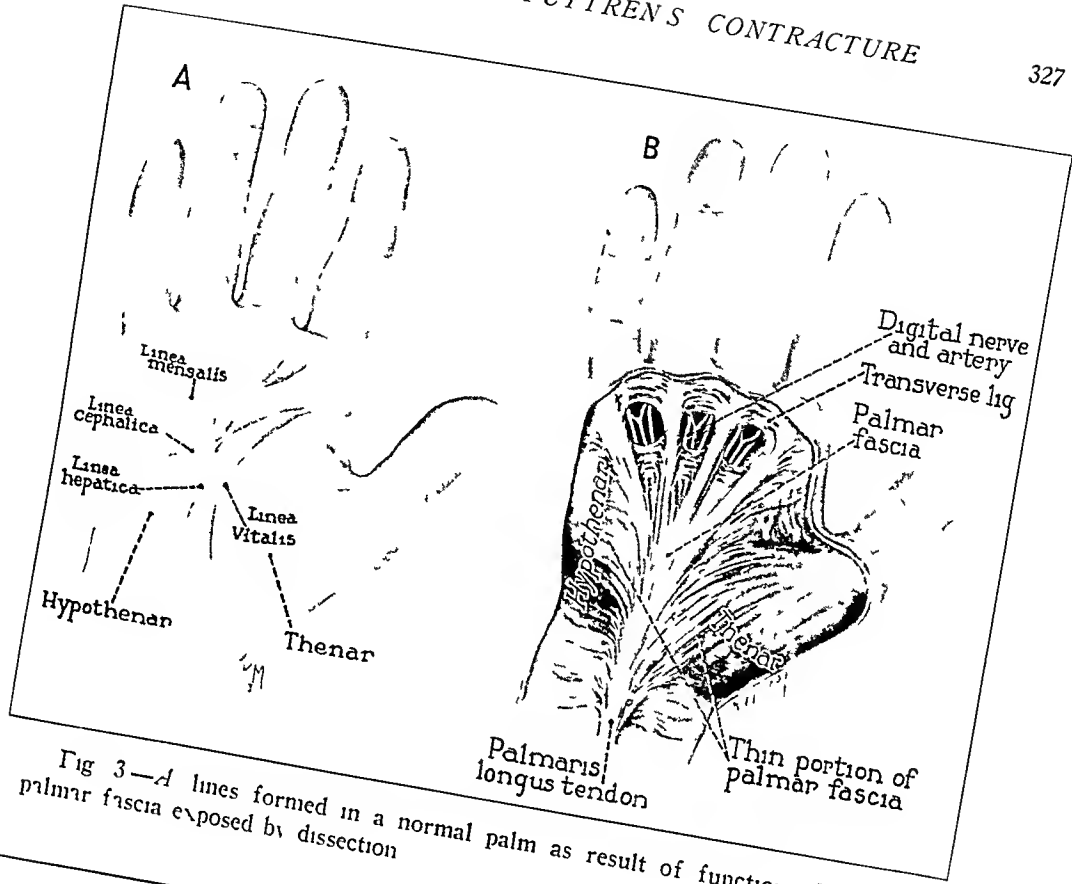


Fig 3—*A* lines formed in a normal palm as result of function, *B* normal palmar fascia exposed by dissection

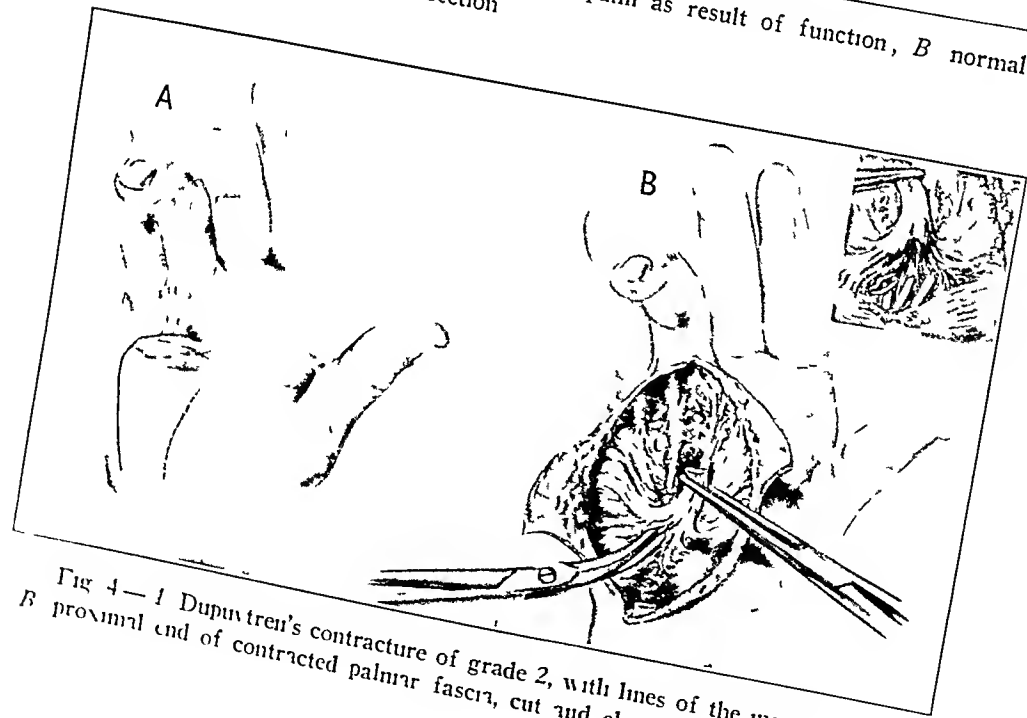


Fig 4—*A* Dupuytren's contracture of grade 2, with lines of the incisions used, *B* proximal end of contracted palmar fascia, cut and elevated

# THE EFFECTS OF CONSTRICTION AND RELEASE OF AN EXTREMITY

AN EXPERIMENTAL STUDY OF THE TOURNIQUET

HARWELL WILSON, M D

AND

NORMAN W ROOME, M D

CHICAGO

Tourniquets have long been used for the temporary control of bleeding from traumatic wounds of the extremities, and chiefly since the time of von Esmarch,<sup>1</sup> to render an extremity relatively bloodless during surgical operations on it. In both instances it is of importance to know how long the constrictor may be left in place with safety to the patient. Various limits have been placed on this period of safety, commonly it is from 1½ to 2½ hours<sup>2</sup> although there are isolated examples of longer constrictions without injury.

The most obvious danger of prolonged constriction is that of interference with the nutrition of the part sufficient to cause subsequent gangrene. Paralysis of the extremity and Volkmann's ischemic contracture are occasionally described<sup>3</sup> as a result of constriction, although Brooks<sup>4</sup> was unable to produce experimental contractures by long periods of ligation. Since the paralyses may occur after relatively short periods of constriction, several authors believe that direct pressure on the nerve trunks is the cause and advocate the use of the pneumatic tourniquet as a safeguard.<sup>5</sup>

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From the Department of Surgery of the University of Chicago

The study was aided by a grant from the Douglas Smith Foundation for Medical Research of the University of Chicago

1 von Esmarch, F. Ueber künstliche Blutleere, Verhandl. d. deutsch. Gesellsch. f. Chir. **2** 1, 1896

2 Matas, R. Surgery, Its Principles and Practice, edited by W. W. Keen, Philadelphia: W. B. Saunders Company, 1909, vol. 5, p. 190, quoted by Reid, M. R., and Andrus, W. D. Surgery of the Arteries, in Nelson Loose-Leaf Living Surgery, New York, Thomas Nelson & Sons, 1927, vol. 1, chap. 12, p. 676

3 Auchincloss, Hugh. Surgery of the Hand, in Nelson Loose-Leaf Living Surgery, New York, Thomas Nelson & Sons, 1927, vol. 3, chap. 5, p. 509

4 Matas<sup>2</sup> Auchincloss<sup>3</sup>

5 Brooks, Barney. Pathologic Changes in Muscle as a Result of Disturbances of Circulation. An Experimental Study of Volkmann's Ischaemic Contracture, Arch. Surg. **5** 188 (July) 1922

6 Eckhoff, N. L. Plea for the Extended Use of the Pneumatic Tourniquet, Lancet **2** 343 (Aug. 15) 1931. Bunts, F. E. A Pneumatic Tourniquet, Ann. Surg. **3** 700, 1910

of the use of subcutaneous operations if the involvement is slight. However, it is difficult for me to understand how the contracted fascia, when extensively involved, can be safely and satisfactorily sectioned subcutaneously, in view of the fact that even with good hemostasis and exposure the operation is obviously so difficult.

The strictest aseptic technic must be employed as infection in an extensive wound of the palm would be disastrous. Preliminary preparation by washing the hand thoroughly with soap and water and applying an alcohol dressing the night before operation is excellent, but it has not always been carried out unless the appearance of the extremity has indicated the necessity of it. As a rule I scrub the hand with benzine to remove the oil from the skin, follow this with ether to dry the skin and then apply a coat of tincture of merthiolate or tincture of iodine diluted half with alcohol. Use of this method has been attended with marked success and patients who have undergone this preparation have not had infections.

The wound is closed snugly and without drainage. A posterior splint of aluminum is applied to hold the involved fingers in extension. The splint should be well padded with gauze to protect the skin over the articulations from excessive pressure. If there is difficulty in obtaining full extension of the fingers, it is best to allow them to be slightly flexed and gradually to force them straight. This is accomplished by placing an adhesive band about the tip of the finger and pulling it against the end of the splint. The splint extends upward to about the middle of the forearm and is molded to fit the contour of the arm. Dressings are not changed for a week. When they are changed the gauze, if dry and adherent, is allowed to remain in position, the fingers are inspected for signs of pressure, and the splint is reapplied. The length of time of fixation varies with the extent of the deformity, I prefer to have the incision healed and then begin motion, reapplying the splint for the night until free motion is obtained. When recurrence appears, it usually takes place in those cases in which operation has been performed with apparent success but fixation has either not been applied or has been continued for an insufficient time.

In dealing with some extensive lesions, especially if operations had been performed previously and ankylosis had followed, I have excised the fascia that had undergone contracture and the involved skin and have used the skin from a disarticulated finger as a pedicle graft to cover the denuded palm, the results have been excellent. Cases in which this method has been used usually have been those in which it has been necessary to remedy a poor result of a former operation the finger has been acutely flexed and prognosis for function of the finger has been poor. Operation gives a more speedy and satisfactory result than could be



loss of fluid which was demonstrated in traumatic shock by Blalock,<sup>11</sup> Parsons and Phemister,<sup>12</sup> Roome, Keith and Phemister<sup>13</sup> and others

Few experimental studies have been made on the effects of tourniquets. Paolucci<sup>7a</sup> and Fogliani<sup>7b</sup> found that the release of constrictors applied to one or both thighs of experimental animals for periods in excess of 3 hours frequently resulted in a profound fall of blood pressure and death, these authors considered the absorption of toxic substances the probable cause of death. Fogliani noted swelling of the limb during constriction in some experiments, which was presumably due to collateral circulation through the femur. Churchill<sup>7c</sup> observed depressions of blood pressure in cats following the release of tourniquets applied for shorter periods but drew no definite conclusions as to their causation. The experiments to be described were carried out in

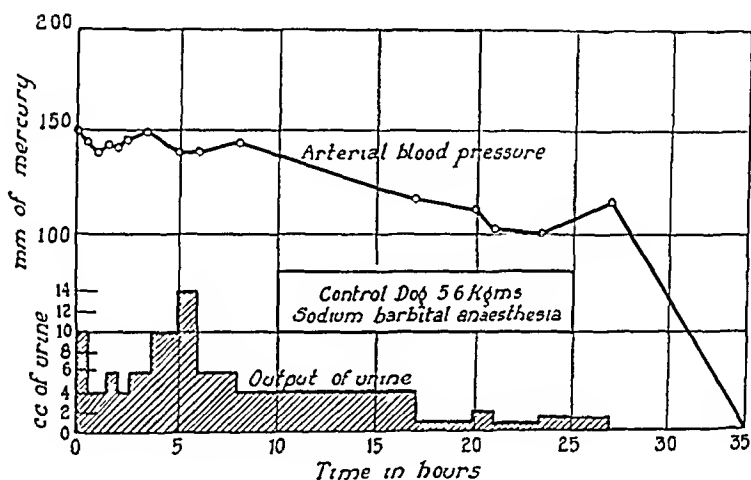


Fig 2—The blood pressure and urinary output of an anesthetized dog. Note that while the blood pressure remains above 100 mm of mercury until shortly before death the urinary output (in cubic centimeters per hour) is markedly diminished after the seventeenth hour.

an effort to evaluate the importance of the various factors in the lowering of the blood pressure and in the causation of death.

#### EXPERIMENTS

*A Control Series*—Six dogs were merely anesthetized with sodium barbitol given intravenously in doses averaging 276.4 mg per kilogram of body weight,

11 Blalock, A. Experimental Shock. The Cause of the Low Blood Pressure Produced by Muscle Injury, *Arch Surg* 20:959 (June) 1930.

12 Parsons, E., and Phemister, D. B. Haemorrhage and Shock in Traumatized Limbs, *Surg, Gynec & Obst* 51:196, 1930.

13 Roome, N. W., Keith, W. S., and Phemister, D. B. The Effect of Bleeding After the Reduction of the Blood Pressure by Various Methods, *Surg, Gynec & Obst* 56:161, 1933.

The cases on which this paper is based were encountered over a period of approximately twenty years, and it is not unlikely that results will continue to improve with improvement in technic and in knowledge of the condition. In estimating the results obtained I have considered that amputation gave a satisfactory result. The results on the 27 hands of the patients who have died or of whom I have lost track can be classified with either the satisfactory or the unsatisfactory results. Thus, if the results secured on these 27 hands are classed with the satisfactory results, the percentage of satisfactory results, in terms of the number of hands operated on, is 91 ( $\frac{106}{117}$ ), if the results on these 27 hands are classed with the unsatisfactory results, this percentage becomes 67.5 ( $\frac{79}{117}$ ). On 97 of the 117 hands the preferable operation, excision of palmar fascia, was performed, and the possessors of 23 of these 97 hands have died or I have lost track of them. If the results on these 23 hands are classed with the satisfactory results, the percentage of satisfactory results, in terms of the number of hands operated on, is 92 ( $\frac{89}{97}$ ), if the results on these 23 hands are classed with the unsatisfactory results, this percentage becomes 68 ( $\frac{66}{97}$ ). If the hands of the patients who have died or of whom I have lost track are omitted from the calculations, the percentage of satisfactory results from all the operations is 88 ( $\frac{79}{90}$ ), and the percentage of satisfactory results from excision of the palmar fascia is 89 ( $\frac{66}{74}$ ).

#### ABSTRACT OF DISCUSSION

DR SUMNER L. KOCH, Chicago. From the time of Platter, of Sir Astley Cooper and of Dupuytren himself Dupuytren's contraction has attracted attention. Kärnel several years ago emphasized the fact that as the contraction involves the finger it also involves the digital nerves and blood vessels. As the contracting cord deviates toward one side or the other it can actually displace the blood vessels and nerves the width of a finger and this makes it easy, as one follows the fascial cord or band into the finger to excise displaced digital blood vessels and nerves before one realizes what has happened. Michael Mason, of Chicago, showed that the digital nerves and blood vessels in the finger lie between two fascial layers. Both are involved in the contracting process. As the fascia thickens and as it draws the finger into a flexed position the digital nerve and blood vessels lie at the very center of the contracting cord. Even if the cord lies parallel with the long axis of a finger if one begins the dissection in the palm follows the thickened fascia distad and removes it *en masse*, one will remove the nerve and blood vessels with it. To avoid such an accident it is necessary to isolate the blood vessels and nerves in the palm and by careful dissection follow them distad to the point where they lie free in normal tissue.

Not only is the superficial palmar fascia involved in Dupuytren's contraction but its extensions dorsad and its connections with the deep fascia of the palm also become thickened and fibrosed. It has been the experience of my associates and my own experience that unless the longitudinal septums which pass dorsad from the deep surface of the palmar aponeurosis are removed the result will not be as satisfactory as one might wish.

of the limb during the period of constriction, the findings thus differing from those of Fogliani,<sup>7b</sup> who presumably constricted at a level permitting collateral circulation. In all cases a marked swelling of the limb gradually developed during the hours following the release of the constrictor. Of the 6 animals surviving periods of constriction of from 2 to 6½ hours, none presented gangrene of any portion of the ligated extremity, although there was a paralysis of varying duration in all. In the animals dying as a result of the procedure, the hind quarters were removed after the method of Blalock<sup>11</sup> as follows. A transverse cut was made through the lower part of the abdomen just above the iliac crests and continued through the lower lumbar vertebrae, the hind quarters were then separated through the midline and the unpaired structures discarded. The symmetrical quarters thus obtained were weighed, and the difference in weight was calculated as a percentage of the body weight. In 11 experiments cultures were made just after

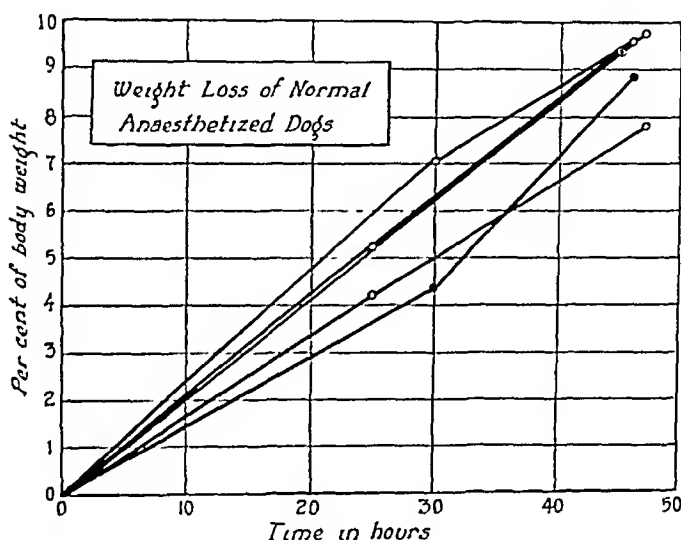


Fig. 3—The loss of weight of anesthetized dogs as a function of the elapsed time

death from small pieces of muscle and areolar tissue from both thighs by grinding with sand and inoculating aerobic and anaerobic mediums.

At necropsy the ligated legs were grossly swollen, boggy and discolored. On incising the skin a fluid escaped, in some cases clear and straw-colored, in others blood-tinged. This fluid was analyzed in 2 cases of this series and in 1 case of series D, with the following results. In that from dog 868, the leg of which was constricted 5½ hours, the nonprotein nitrogen was 46.9 mg per hundred cubic centimeters, proteins, 2.6 Gm, and chlorides, as sodium chloride, 603 mg. In that from dog 273, the leg of which was constricted 14¾ hours, the proteins totaled 5.42 Gm per hundred cubic centimeters and chlorides, as sodium chloride, 566 mg. In that from dog 583, the leg of which was constricted 7 hours, the proteins totaled 5.3 mg per hundred cubic centimeters and chlorides, as sodium chloride, 689 mg. In 3 cases gas bubbles were observed in the tissues and crepitation was felt.

with acute arthritis. The muscle tendon of the palmaris longus above the wrist became thickened. The patient has never completely recovered the use of this hand.

Another patient had suffered a compound fracture of the jaw. Chronic osteomyelitis followed. Pus discharged from the jaw for more than a year. During this period Dupuytren's contracture developed in both hands.

Therefore, it is evident that Dupuytren's contracture should not invariably be treated by an immediate operation. In all cases, with slowly or rapidly progressive course, the etiologic factors should be studied and eliminated, if possible. Operation may be performed later, if necessary.

The operation that I described in 1919 consisted in the complete excision of the palmar fascia through the distal palmar transverse crease. If the fascia of the fingers is involved, it is to be excised through a transverse incision along the crease at the base of the finger. I object to incisions in the hand which extend counter to the natural creases.

By this method of operation I have never failed to secure a complete and permanent cure except in the case in which active arthritis of the hand developed.

I agree with Dr. Meyerding that the skin of the palm should never be sacrificed. I have never found it necessary to transplant skin to the hand.

of the two legs (fig 4), proving the absence of arterial thrombosis. No venous thrombosis was found in any case on dissection.

*C. Plethysmographic Studies*—Three animals (457, 458, 459) anesthetized with sodium amital or sodium barbital intravenously were studied to determine the

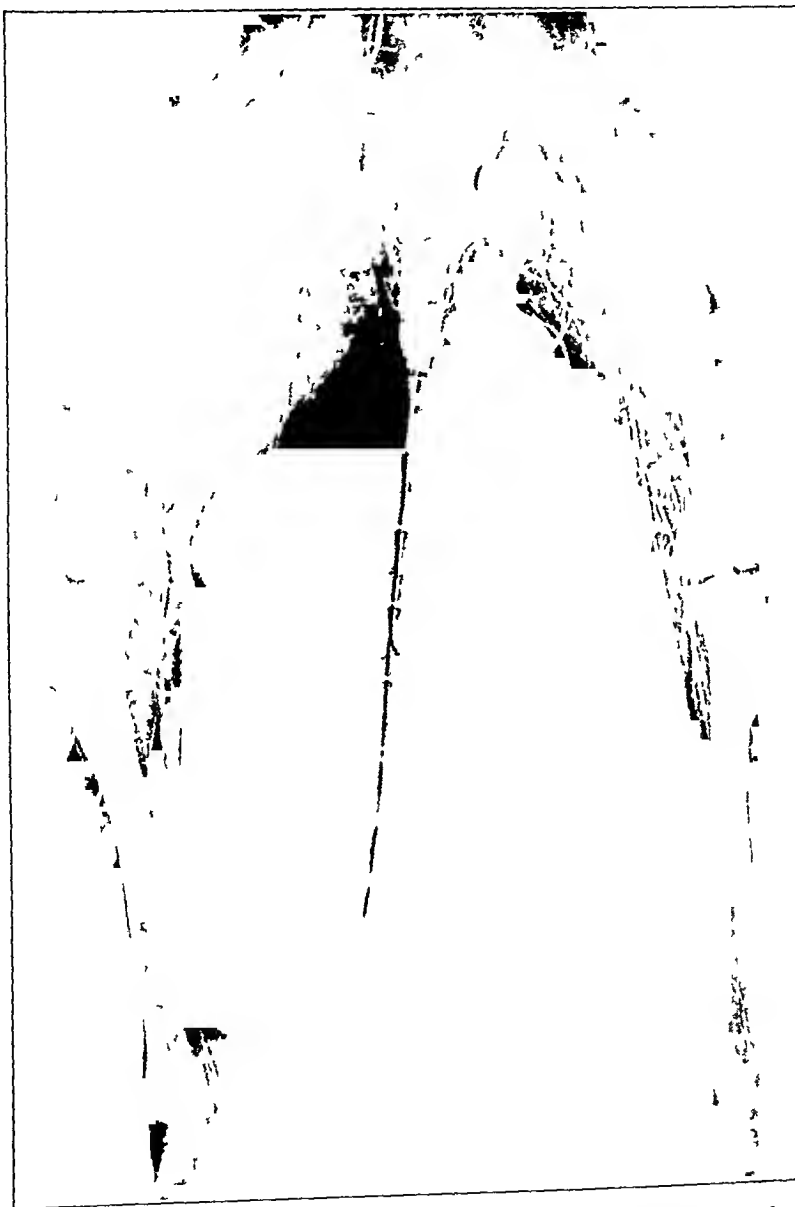


Fig 4—Arteriogram of the hindlegs of a dog, one of which (at left in the figure) had been ligated for 9 hours. A show-card color solution was injected into the blood vessels and an x-ray film made 8 hours after release of the constriction. Note the swelling of the ligated leg and the nearly equal filling of the arterial tree in each leg.

effect of release of the obstructed blood supply to a limb on the general vasomotor tone. In each dog one hindleg was prepared by severance of all tissues, high in

Another danger is the circulatory depression which has been observed<sup>7</sup> to follow the release of a constrictor. There are usually a sharp primary fall in blood pressure with rapid recovery to nearly the previous level and a more gradual secondary fall over a period of hours. Examples of this characteristic curve of the blood pressure are given in figure 1. The explanation of the depression of the blood pressure and of its characteristics seems to depend on one or more of the following factors, viz (1) the return of the normal volume of blood to the limb, if the blood was expressed during the application of the tourniquet, (2) reactive hyperemia of the limb, as described by Bayliss,<sup>8</sup> (3) the absorption of toxic metabolites into the general circulation in a manner similar to that of the absorption of toxic materials from traumatized tissues as is thought to occur by Cannon,<sup>9</sup> Moon and Kennedy<sup>10</sup>

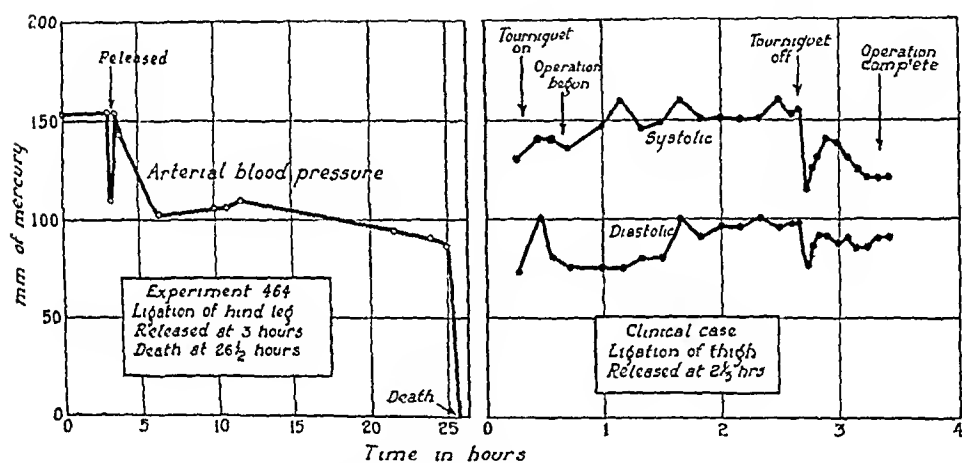


Fig 1—The characteristic effects on the blood pressure of the release of a tourniquet in an experimental animal (at left) and in a patient (at right). Note the sharp depression on release with rapid recovery, and the more gradual secondary fall.

and others, and (4) swelling of the limb, after restoration of the circulation, by transudation of a plasma-like fluid, similar to the local

7 (a) Prolucci, R. Fenomeni di shock da prolungata costrizione di laccio emostatico, *Arch. ital. di chir.* **21** 329, 1928. (b) Fogliani, U. Sulla patogenesi dello shock sperimentale da laccio emostatico, *Riv. di pat. sper.* **9** 257, 1932. (c) Churchill, E. D. Communication to the Society for Clinical Surgery, Boston Meeting, Nov. 14, 1931.

8 Bayliss, William. *Principles of General Physiology*, ed. 4, London, Longmans Green & Co. 1924, p. 703.

9 Cannon, W. B. *Traumatic Shock*. New York: D. Appleton & Company, 1923.

10 Moon, A. H. and Kennedy, P. I. Pathology of Shock. *Arch. Path.* **14** 360 (Sept.) 1932.

time the leg was markedly swollen in each case. The amputation was followed by the administration of large amounts of whole blood at intervals. These animals survived, being killed at 5 and 7 days.

Two other animals (11 and 12) were treated by amputation of the ligated leg at the level of constriction  $3\frac{1}{2}$  and  $3\frac{3}{4}$  hours after release, without administration of blood or other fluids. These died at 8 and 32 hours after release, respectively.

#### COMMENT

In series B of the experiments described it was observed that 69 per cent of the dogs died after the release of a constrictor applied to one hindlimb for periods of from 2 to 20 hours, while only 17 per cent of a control series (series A) died from the prolonged anesthesia and fast of a similar period of observation. When the constrictor is released (fig. 1) there is a very transient fall of the blood pressure, with recovery, followed by a more gradual and more pronounced fall which continues in the experimental animal until death occurs. The primary fall is probably due to reactive hyperemia and to the absorption of metabolites into the general circulation, since in series C a fleeting minor vasodilatation was demonstrated in the opposite limb.

But it is the secondary gradual depression of the blood pressure with which we are principally concerned, since it is sustained and seems to be related to the cause of death from constrictor release. The chief causes to be considered in explanation of this secondary fall and of the mortality from the release of a tourniquet are as follows: (1) the formation of toxic tissue metabolites or of the products of anaerobic bacteriolysis in the ligated limb and their absorption on release, (2) the withdrawal of fluid from the circulation to be poured out into the limb as a transudate in sufficient quantities to embarrass the general circulation. It was shown by dissection and by roentgenographic studies that the vessels of the ligated limb remain patent so that either of the factors mentioned might be effective.

In regard to the question of the absorption of toxic metabolites from the damaged limb, it seems that their concentration would be greatest immediately on release of the constrictor and would then diminish rapidly as circulation continued through the limb. Death from this cause would therefore be expected to occur soon after the reestablishment of the circulation through the limb, but such is not the case, since the animals died on the average  $25\frac{3}{4}$  hours after release. On the other hand, this interval of time is compatible with the depletion of the blood volume by the slow process of transudation either generally or locally into the limb. It was shown in the experiments that a large loss of fluid occurs locally, it is thought, therefore, that the effect of the absorption of metabolites is combined with the effect of reactive

and their weights were observed at intervals over periods of from 45 to 47 hours, during which no food or fluid was given. At the end of this period of observation the animals, which had regained consciousness, were returned to cages, watered and fed.

In control animal 712 a catheter was introduced into the urinary bladder and all the urine collected. The total loss of weight was 0.469 Kg, 110 cc of urine was obtained during the first 20 hours and none thereafter. In another animal, not included in the series, direct measurements of blood pressure were made periodically, and the output of urine through a cystostomy was measured at half-hour intervals; the results of this experiment are summarized in figure 2. This graph shows that the blood pressure gradually fell but did not reach a low level until shortly before death, and that the urinary output fell nearly to zero after 17 hours. The total urinary output was 107 cc, the total loss of weight, 0.5 Kg. The animal died at 35 hours, a factor in causing death was the repeated small withdrawals of blood necessitated by the use of a carotid cannula, for which reason this animal was discarded from the group of controls.

Of the 6 animals studied, all but 1 (871) survived (table 1). The animals lost weight in almost direct proportion to the elapsed time, the average amount being 9.11 per cent of the body weight in 46½ hours (fig. 3). This loss of weight

TABLE 1—Control Series

Dog	Dose of Barbitol Sodium, Mg per Kg	Loss of Weight, per Cent of Body Weight	Result
712	285	9.4% at 45 hours	Recovery
841	271	7.8% at 47 hours	Recovery
845	276	9.8% at 47 hours	Recovery
871	277	8.9% at 46 hours	Death at 64 hours
82	270.5	9.65% at 46 hours	Recovery
820	279	Not weighed	Recovery
Average	276.4	9.11% at 46½ hours	

occurring in the absence of food or fluid intake was due chiefly to evaporation from the respiratory tract, since in the two animals in which the urinary output was measured this amounted to only one fifth to one fourth of the total loss of weight and since none of the animals defecated during the period of observation. These results coincide well with the studies of Coller and Maddock,<sup>14</sup> who found that surgical patients lost as "insensible loss of water" from 1.6 to 4.5 per cent of their body weight daily.

*B Constriction Experiments*—Nineteen dogs were anesthetized with similar doses (actual average, 262.4 mg per kilogram of body weight) of sodium barbitol intravenously, and one hindleg was constricted in the following manner for periods of from 2 to 20 hours. A slender steel skewer about 12 cm long was placed through the gluteal muscles with aseptic precautions, and two turns of rubber tubing were tightly applied above the pin at the level of the hip joint, thus minimizing collateral circulation through the femur. The animals were weighed before and at intervals during the experiments.

Of the 19 animals studied, 6 recovered while 13 died at intervals of from 5 to 52 hours after release of the constrictor. There was in no case noticeable swelling

<sup>14</sup> Coller, F. A., and Maddock, W. G. The Water Requirements of Surgical Patients. *Ann Surg* 98:952, 1933.



The administration of blood or plasma to the animal in amounts approximately equal to the estimated loss of fluid into the ligated extremity was found to be insufficient to prevent death after prolonged constriction. The reason for the failure of this method of treatment was apparently that the blood or plasma administered did not remain in the general circulation but was poured out into the damaged limb as an increased amount of transudate, where it was, in part, recovered in the experiments. When this leakage was prevented by amputation, transfusion of blood caused survival. Amputation of the ligated leg without the administration of blood or plasma was shown to be inadequate to prevent death when performed after swelling of the leg had occurred.

#### SUMMARY

Experiments were performed on 19 dogs in an effort to study the effects of prolonged constriction of a limb. One hindlimb of each dog was ligated by means of a rubber tourniquet for a period of from 2 to 20 hours under barbital anesthesia and then released. Of these animals 69 per cent died at an average interval of 25 $\frac{3}{5}$  hours after release of the constrictor, while only 17 per cent of a control series died. No animal with a leg constricted for less than 3 hours died, while every animal with a leg constricted for a period in excess of 6 $\frac{1}{2}$  hours died.

The possible reasons for the depression of blood pressure which follows the release of a tourniquet and for the subsequent death of the animal were discussed. It was thought that reactive hyperemia of the constricted limb and the absorption of metabolites from the limb were probably responsible for the primary transient depression of the blood pressure, but that the secondary and more serious fall of blood pressure was occasioned by swelling of the damaged extremity by transudation and the consequent diminution of the circulating blood volume. The local loss of a part-plasma fluid in amounts probably adequate to cause death was demonstrated. The absorption of the products of anaerobic bacteriolysis of the tissues is another possible factor in the lowering of the blood pressure, but no positive proof or denial of its importance can be adduced from the present experiments. Survival of the animal after prolonged constriction of a limb was obtained by amputation of the limb followed by transfusion of blood, but not by transfusion alone or by amputation alone.

#### CONCLUSIONS

- 1 Prolonged constriction of an extremity by a tourniquet and release result in circulatory depression and death in a high percentage of dogs. The mortality increases with increased periods of constriction.

The results of these experiments are summarized in table 2. It will be observed that 6 dogs survived after the release of constrictions of from 2 to 6½ hours, while 13 dogs died after constrictors which had been applied from 3 to 20 hours were released. These animals died from 5 to 52 hours after release, the average of the survival periods being 25½ hours. There was an average net loss in weight of 4.26 per cent during this period, which is approximately the same as that observed in the control series. There was an additional loss of fluid into the constricted extremity averaging 3.54 per cent of the body weight at the time of death. An anaerobic gas-forming bacillus was recovered from the normal leg in 7 of 11 cases, and from the ligated leg in 8 of 11 cases, no specific identification of this Clostridium was attempted.

TABLE 2—Results of Constriction Experiments

Dog	Dose of Barbitol Sodium Mg per Kg	Duration of Constriction, Hours	Survival After Release, Hours	Net Loss of Weight at Death per Cent of Body Weight	Loss of Weight Into the Extremity per Cent of Body Weight	Cultures*	
						Normal Leg	Constricted Leg
1	203	2	Recovery				
2	203	2.5	Recovery				
4	270	3	26.5	0.54	7.17		
892	271	3.25	52	7.4	2.3	+	+
3	260	3.5	33	2.41	3.13	—	+
792	272	4	36	7.2	1.0	—	—
755	263	4	Recovery				
86	272	5	14	3.45	3.0	+	+
153	279	5.25	11	5.1	6.1	+	+
807	274	5.5	Recovery				
868	271	5.5	20	2.2	4.3	+	+
20	273	5.5	44	0.9	2.5	+	+
754	261	6	Recovery				
921	†	6.5	Recovery				
5	270	7	8	2.0	2.1	—	—
6	202	8	47	3.25	4.61		
712	268	8	25.5	4.4	5.6	+	—
273	294	14.75	5	3.93	3.1	—	+
283	276	20	13.5	5.9	5.25	+	+
Average	262.4		25.6	4.26	3.54		

\* A plus sign indicates the presence, a minus sign the absence, of Clostridia.

† Given saline solution two hours before death; this figure is not included in the average.

‡ Morphine used.

dium was attempted. Various other organisms were cultured infrequently and irregularly from both legs.

The question as to whether thrombosis or occlusion of the vessels occurred in the constricted limb was investigated by dissection of the limb in most of the animals of the experimental series, and by the following studies on 3 dogs that were not included in the series. One hindleg of each was ligated as described for periods of 3¼, 5 and 9 hours. When the animals were apparently moribund, 14, 15 and 8 hours, respectively, after the release of the constrictor, the aorta was cannulated, the dog bled from the carotid artery, and a mixture of vermilion show-card color (mercuric sulfide) and water was injected at once into the distal aorta. Roentgenograms showed very nearly equal filling of the arteries

# THE PRESENT STATUS OF IODINE IN TREATMENT OF EXOPHTHALMIC GOITER

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The value of iodine in the preoperative treatment of exophthalmic goiter is too well established to admit of any controversy. Since Plummer almost twelve years ago put forward his advocacy of aqueous solution of iodine U. S. P. administered in connection with the treatment of this condition there has been a steady increase in the employment of this therapy and a corresponding increase in the success which has attended therapy of goiter in general, attributable largely to iodine medication. So great indeed has this success been that there is perceptible at present a tendency to overdo iodine medication and to make use of it as routine in all cases in which dysfunction of the thyroid has been postulated or even suspected, without due consideration of possible contraindications or a real understanding of all the factors involved.

This tendency is much to be deplored, for it will inevitably lead to a revolt against the apparent misapplication of a valuable therapeutic adjuvant simply because it has failed to prove itself a specific for every manifestation of disease of the thyroid. There seems to be little in the recent literature which sounds any such note of warning, nor have I encountered detailed discussions of the limitations which an extended use of aqueous solution of iodine as a preparative measure in the surgical treatment of exophthalmic goiter has taught the medical profession to respect most strictly.

An exception to this is the paper by Martin<sup>1</sup> of Montpellier, which appeared in the *Archives de la Société sciences Médicales du Montpellier* in March last year. In this paper stress was laid on the advantages of iodine medication in early life. For simple goiter it is recommended "invariably" for children, "under careful surveillance" for adolescent boys and girls, "with extreme prudence" for persons over 25 and "never after 40 except at the risk of producing Basedow's syndrome." But as preparation for operation when exophthalmic goiter is already established, its "prudent employment in small doses and for a very limited time" is allowable, although the author concluded by stating his opinion that its value is to be questioned in any case of

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1 Martin, J. Iode et goîtres, Arch. Soc. d. sc. med. et biol. de Montpellier

the thigh, except the femoral artery and vein and the femoral and sciatic nerves. The artery and vein were obstructed for periods of from 2 to 2½ hours and then released. A plethysmograph applied to the opposite limb and connected to a sensitive piston recorder showed in all cases a transient minor vasodilatation of 0.2 cc or less and of about a minute's duration.

*D Transfusion and Amputation Experiments*—Eight experiments, summarized in table 3, were carried out in an attempt to prevent by treatment such deaths as were observed in series B following prolonged constriction of a limb. The anesthesia and method of constriction were in all cases exactly similar to those of series B.

In 2 animals (583 and 585) a limb was constricted for 7 and 10 hours, respectively, and the animals were treated with very large amounts of citrated whole blood, given in repeated small doses at intervals, and usually accompanied by

TABLE 3—*Transfusion and Amputation Experiments*

Dog	Weight of Dog, Kg	Duration of Constriction, Hours	Treatment Given	Survival After Release, Hours	Loss of Weight Into Extremity, per Cent of Body Weight	Cultures*	
						Normal Leg	Constricted Leg
585	10.6	10	340 cc of citrated blood and 375 cc of physiologic solution of sodium chloride at intervals intravenously	16	7.75	—	+
583	10.2	7	480 cc of citrated blood and 200 cc of physiologic solution of sodium chloride at intervals intravenously	7	3.98	—	—
7	7.9	7	640 cc of citrated plasma at intervals intravenously	30½	6.0	—	+
8	8.4	7	500 cc of citrated plasma and 200 cc of physiologic solution of sodium chloride at intervals intravenously	12½	6.55	—	—
9	9.2	10	Amputation 1½ hours after release, and 500 cc of citrated blood intravenously		Recovered		
10	13.4	7½	Amputation 4 hours after release, and 615 cc of citrated blood intravenously		Recovered		
11	8.0	8	Amputation 3½ hours after release	8			
12	8.8	7¾	Amputation 3¾ hours after release	32			

\* A plus sign indicates the presence a minus sign the absence, of *Clostridia*.

physiologic solution of sodium chloride (table 3). These animals died 7 and 16 hours after the release of the constrictor. Two dogs (7 and 8) each had a limb constricted 7 hours, and likewise died in spite of the administration of very large doses of citrated plasma. In these 4 experiments in which death occurred after the replacement of blood or plasma in apparently adequate amounts, there was a marked increase in the loss of fluid into the ligated extremity as compared with the losses observed in series B, the average amount being 5.77 per cent of the body weight. Thus, it appeared that much of the fluid administered failed to remain in the general circulation, but instead was poured out into the tissues of the damaged limb.

Therefore, in 2 animals (9 and 10) amputation of the ligated leg at the level of constriction was done 1½ and 4 hours after release of the tourniquet, at which

tunes a day—and the results obtained, we believe, fully justify us in continuing this course. Though we prefer the aqueous solution, there is no reason to stress the *importance* of one form of iodine over another. We do think, however, that inorganic iodine is superior to the di-iodotyrosine preparations concerning which one heard so much several years ago. It may be remembered that Gutman and his associates<sup>2</sup> at the Medical Center, New York, used this treatment in thirty cases of hyperthyroidism in which operation was to be performed, while maintaining a careful comparison with another series of cases in which aqueous solution of iodine or sodium iodide was administered. In their conclusions Gutman and his co-workers stated that they were more impressed by the similarities than by the differences between the response of patients with hyperthyroidism to di-iodotyrosine and the response to other iodine compounds, and in the end these workers decided that the conclusion that the effects of the two forms of medication are essentially the same “appears justified.”

I have reason to believe that the fear that the administration of large doses will cause iodine hyperthyroidism is groundless. I will even go so far as to say that the existence of any such entity as hyperthyroidism caused by iodine appears problematic. It is reasonable to suppose that if one were to give large quantities of iodine over a long period iodism might occur and the good effects which the iodine medication unquestionably has on the disturbance in the thyroid would in this way be obscured, even to the extent of simulating overactivity of the gland. But we have never observed such a case.

As to the time which should be occupied in administering a course of iodine therapy, my colleagues and I are again in disagreement with the French surgeon whom I quoted. In clinical work we have found that from ten days to two weeks is usually sufficient for patients whose glands are only moderately enlarged. The size of the gland is the criterion, not the severity of the symptoms. Observations made during the period of administration of iodine will serve to establish the length of time medication should be continued. In patients with the large hyperplastic type of gland we watch for local changes in the thyroid itself and observe their relation to the abatement, or failure to abate, of the characteristic symptoms. In cases of this general type it is sometimes deemed wise to give iodine for as long as four weeks before considering the patient sufficiently prepared for operation.

These remarks apply only to the use of iodine as a measure of pre-operative preparation. The long continued employment of iodine when surgical intervention is not contemplated is another matter. In this

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<sup>2</sup> Gutman, A. B., Sloan, L. W., Gutman, E. B., and Palmer, W. W. Role of Diiodotyrosine in Hyperthyroidism. A Comparison of Therapeutic Effect of Diiodotyrosine with Inorganic Iodine, *J. A. M. A.* **101**: 256 (July 22) 1933.

hyperemia to cause the primary transient fall of the blood pressure, and that it is not important in the causation of the more serious secondary fall

No definite conclusion can be reached from the present experiments as to the importance of the products of bacterial action in the limb in the causation of death. Clostridia were demonstrated in the tissues of both the normal and the constricted legs in a majority of the experiments, but no tests were made as to the production of exotoxin by the strains recovered. But, in view of the work of Trusler and Reeves,<sup>15</sup> it is possible that these organisms are not identical with *Clostridium Welchii* and do not form a true exotoxin. However, the "muscle organism" described by these authors formed gas and liquefied tissues much as *C. Welchii* does, and the products of this disintegration of tissue may be circulatory depressants.

The possibility that death is due to the withdrawal of fluid from the circulation to produce swelling of the limb seems likely from the experimental data presented. By calculation of the difference in weights of the two hind quarters it was found that an average accumulation of fluid equal to 3.54 per cent of the body weight had occurred in the constricted limb. This fluid had chemical characteristics showing that it was, in large part, plasma. It has been shown by Blalock<sup>16</sup> that loss of plasma is lethal when it is removed in small amounts totaling on the average 2.4 per cent of the body weight over an average period of 28½ hours. It is thought, therefore, that the amount of part-plasma fluid lost into the constricted limb in the present experiments is adequate to cause death.

A contributory cause of death in experiments of this type is the long period of anesthesia during which no food or fluids are given. There was found an average loss of weight, chiefly from the respiratory tract, of 4.26 per cent of the body weight during the average period of 25¾ hours; this loss of water no doubt constitutes a sensitization to further loss of fluid, as into the constricted limb.

The animals of series B fall into three groups, as follows: (1) those in which the limb was constricted for periods of less than 3 hours, all of which recovered, (2) those in which the legs were ligated from 3 to 6½ hours, of which some died and some recovered, and (3) the group in which constriction was for periods longer than 6½ hours, all of which died. Thus, the mortality from ligation and release of an extremity increases with the duration of ligation.

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<sup>15</sup> Trusler, H. M., and Reeves, J. R. Significance of Anaerobic Organisms in Peritonitis Due to Liver Autolysis, *Arch. Surg.* **28**: 479 (March) 1934.

<sup>16</sup> Blalock, A. Experimental Shock, *South. M. J.* **23**: 1013, 1930.

These are the patients who later seek treatment in the well known clinics for the treatment of goiter. The surgeon to whom they eventually are assigned is faced with a grave problem. He must perform the operation under risks practically as great as those taken before the therapy with aqueous solution of iodine was devised. For the "iodine-fast" patient a primary thyroidectomy is too dangerous. Lobectomy or ligation must be resorted to, and the long delay and uncertain outcome add greatly to the anxiety of all concerned.

In view of these clinical observations, the probability that the thyroid, like the pituitary gland, secretes two distinct hormones becomes strong. Kendall's<sup>5</sup> work of almost two decades ago established the existence and action of a compound which has since been termed thyroxine. At the time this experimentation was being carried on, it was demonstrated that in cases of complete atrophy of the thyroid, when the basal metabolic rate is 40 per cent below normal, the administration of thyroxine alone will restore the rate to normal and maintain it as long as the extract is taken regularly. In commenting on this Kendall put the question: In complete atrophy of the thyroid, the complete or nearly complete absence of thyroxine may be assumed, therefore, what maintains energy output from 100 per cent below normal, which would be death, up to 40 per cent below normal, the point to which basal metabolism sinks in the absence of thyroxine?

Kendall was able to answer this question only by propounding another, which he used as the conclusion to a paper on the subject of thyroxine in 1918:

That the active [chemical] groups present in thyroxin are a necessary mechanism for the production of energy within the body seems highly probable, and it is of great interest and significance that there exists a close analogy between this substance, whose exact effect on metabolism we know, and other substances, creatin, creatinin, amino-acids and proteins, which are also intimately associated with reactions occurring within the animal organism. Are these substances also concerned in the maintenance of the basal metabolism?

So far as I know, no one has attempted to answer this or allied questions until recently. A year ago, Davis<sup>6</sup> sought to establish what it is that binds iodine to form the active principle of the thyroid, thyroxine. His method was suggested by Sweet's article in 1918, in which it was related that a type of colloid goiter could be developed in dogs by ligation of the pancreatic duct. This suggested that the removal of trypsin from the intestinal tract brought about incomplete hydrolysis of the proteins to the amino-acid stage. In this event tyrosine would

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5 Kendall, E. C. The Active Constituent of the Thyroid, *J. A. M. A.* 71: 871 (Sept. 14) 1918.

6 Davis, J. S., Jr. Thyroid Secretion, *Ann. Surg.* 99: 383, 1934.

2 The fall of blood pressure and death are probably due chiefly to the withdrawal of water and plasma proteins from the general circulation to produce local swelling of the constricted limb

3 Transfusion of blood or amputation of the leg after swelling has occurred are inadequate to prevent death after prolonged constriction. Amputation of the damaged limb followed by transfusion, however, leads to survival



## ADMINISTRATION OF IODINE IN RELATION TO OPERATION

Contrary to the experience of Clute and Pilcher, which may be accepted as the general experience at the Lahey Clinic, my colleagues and I have not had unpleasant occurrences during operation on patients who had been taking iodine for an extended period before they came into our care. Recently I operated on a patient with a large exophthalmic goiter who had been taking iodine, 10 minims four times a day, for six months previously. A bilateral subtotal thyroidectomy was performed, and convalescence was uneventful, with the temperature never going above 102 F.

We continue to administer iodine after the gland has been removed, giving 31 grams (2615 Gm.) of sodium iodide intravenously while the patient is on the operating table. During the first twenty-four hours after operation, about 100 minims (62 cc.) is administered by rectum. If the patient is admitted to the hospital four or five days prior to operation, we keep her in bed and increase the previous dosage of iodine up to 15 minims (163 cc.) three times a day.

I treated thirty-two patients in this way from January to December 1934, with no fatalities. In most cases the operation is completed at one session, but if the goiter is exceptionally large we perform a unilateral lobectomy and remove the second lobe about three days later, closing the wound entirely in the interval between the steps of the procedure. We suture the sternothyroid muscle to the anterior fascia of the trachea but do not use any drainage when the thyroidectomy is completed. As we have performed more than fifteen hundred operations without postoperative drainage, we are convinced that our practice in this regard has proved its wisdom.

If the gland is friable the two stage lobectomy has proved the best method of handling, and we never perform a total thyroidectomy, as we feel that subtotal excision relieves the symptoms of hyperthyroidism and offers no risk of producing those attending myxedema. Subtotal resection is most satisfactory in those patients who give definite evidence of thyroid hyperplasia with hyperthyroidism together with congestive heart failure or angina pectoris. In this type of patient we have had particularly good results and have been able to confer substantial benefit, equal to that following total excision, without subjecting the patient to any of the risks of the more radical procedure.

The administration of iodine must, of course, be carried out under the careful supervision by the physician in charge. Hyperthyroidism does not take place until a rise in the basal metabolic rate has been in evidence for a definite length of time. If toxic symptoms arise it is a sign that the secretion from the thyroid is not normal, in other words, one is dealing with a perverted secretion, not with an increase in the

exophthalmos For one case in which it cures, it aggravates the condition in a far greater number, he wrote

I cannot subscribe to the conclusions of this French author, for during a period of more than a decade my colleagues and I have employed iodine as routine preoperative medication and have noted a steady improvement in postoperative results and a lowering of mortality, which despite greater skill in operative technic can be accounted for by nothing except the virtues of this preoperative medication Therefore, we do not hesitate to state emphatically that iodine should be administered when preparing patients with hyperplastic goiter for operation

#### DURATION AND DOSAGE

In the matter of duration of this preoperative medication as well as the amount to be given, we again differ with Martin, although his method of treatment is based on that followed in Switzerland, where an unparalleled experience with goiter (although mostly of the colloid type) has given physicians an authority which cannot be lightly disregarded Martin advocated fractional dosage 5 drops twice a day or, better, 2 drops five times a day, which acts much better than 10 drops taken all at once

Against this I would contrast our procedure, for despite this and other opinions to the contrary, I do not think that small doses of 1 or 2 minims (0.062 or 0.124 cc) are sufficient We have yet to have evidence presented which will serve to convince us that doses as small as those mentioned will be efficient in producing the stasis in the thyroid activity which is the result sought by such medication We maintain that the chief action of iodine in these cases is mechanical Depletion of the iodine store of the thyroid gland in cases of exophthalmic goiter has been repeatedly demonstrated When one administers iodine in the form of aqueous solution of iodine, U. S. P., there is a rapid increase in the colloid content of the gland This causes backpressure on the glandular acini and cell structure, as well as on the blood vessels by which they are surrounded, thus producing decided edema within the gland This edematous condition is invariably in evidence when one operates on the thyroid of a patient previously treated with iodine It is the mechanical action of the edema which causes a stasis of functional activity in the secreting cells of the glandular tissue Because of this lowered functional activity the amount of toxin poured into the blood stream is shortly diminished, and clinical improvement is soon apparent To bring about this stasis the action of the solution of iodine must be prompt, otherwise its purpose will be defeated

Acting on this line of reasoning, we give large doses of aqueous solution of iodine—sometimes as high as 10 minims (0.62 cc) three

also noted that the constitutional state associated with arteriosclerosis heightens the vagotonic tendency

In a later study,<sup>11</sup> published a few months ago, Sigler presented fifty electrocardiograms obtained of pressure on the carotid sinus, which showed the predominant vagal effects on the heart to be sinu-auricular slowing or standstill and various grades of auriculoventricular block. Pressure on the right carotid sinus had a greater tendency to produce complete standstill.

In his elaborate monograph on the carotid sinus, presented in 1933 at the University of Paris, Merklen<sup>12</sup> gathered a vast array of evidence, on which he commented as follows:

There is special interest in the facts cited here for the surgeon, particularly for him who is called on to operate in the region of the neck. In cases of goiter or cervical tumor it is shown to be important to avoid all traction and irritation of the carotid arteries, which points to cocainization of the sinus being preferable to chloroform or ether anesthesia, as either of these forms of anesthesia may exaggerate still further the sinocarotid reflexes.

It would seem that the vagotonic predisposition may have been present in our cases of unexplained death. This question should have further investigation.

#### CONCLUSIONS AND SUMMARY

1 Iodine has definite but limited value in the treatment of hyperplastic goiter. It is used preferably in preoperative preparation.

2 The period of preoperative iodinization should last from ten days to two weeks when the gland is of moderate size, regardless of the severity of the symptoms. Considerable dosage is required.

3 The use of iodine for treatment without thyroidectomy in view has the unfortunate effect of making the patient "iodine-fast," so that when operation finally becomes necessary preoperative iodinization fails to produce the temporary benefit required to reduce surgical risk.

4 The temporary improvement following iodine medication in cases of exophthalmic goiter is due to the deposition of colloid and edema of the gland, causing backpressure on the glandular acini which checks toxic absorption. When compensation occurs in the gland the toxic symptoms reappear.

5 Sudden death on the operating table continues to occur as a result of surgical intervention on the thyroid. We have had five such deaths in the course of performing over eight thousand thyroidectomies.

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11 Sigler, L. H. Electrocardiographic Observations on Carotid Sinus Reflex, *Am Heart J* 9 782, 1934.

12 Merklen, E. P. *Recherches cliniques et experimentales sur le sinus carotidien*, These de Paris, no 137, 1933.

respect we are in complete agreement with Clute and Pilcher,<sup>3</sup> who stated about a year ago

Surgery is a safe, quick, and sure method for the cure of hyperthyroidism. The longer the hyperthyroidism persists, whether it be partially controlled by iodine or not, the more serious the disease and the more dangerous the surgery. We are completely satisfied that it is wrong to give patients with hyperthyroidism, whether it be due to exophthalmic goiter or to adenomatous goiter, iodine for long periods of time, before insisting upon the surgical treatment.

Many of Clute and Pilcher's patients came to them after they had had long courses of treatment with iodine elsewhere. Indeed, it was doubtless the failure of this treatment that led their previous medical attendants to "give them up," so that they eventually reached the Lahey Clinic as greater surgical risks and generally in much poorer condition than the patients who were under care in this clinic from the onset of hyperthyroidism and received iodine medication for only a limited period and purely as a preoperative measure.

Clute and Pilcher were led to conclude that one of the greatest evils done by iodine is the influence of an initial gain under such medication "in misleading the patient and postponing, in certain cases, the necessary surgical measures in potentially malignant non-toxic goiters. The administration of iodine for long periods of time in hyperthyroidism does great harm in increasing the risk of surgery, the number of operations necessary for the relief of the patient, and the prolongation of the patient's disability."

As far back as 1928 Jackson<sup>4</sup> emphasized the grave possibilities of this situation. He found that although iodine effected a temporary benefit in cases of exophthalmic goiter this was followed by a period in which the patient became "iodine-fast" and acquired a tolerance for the drug. The metabolic rate, which at first had fallen with such gratifying promptness, again became elevated, and in some instances the myocardium was so damaged that auricular fibrillation occurred. In the meantime the general appearance and well-being of the patient improved temporarily. The weight increased, and in the patient's own opinion he was deriving great assistance from the medication. This period of improvement, however, was variable. Some patients responded very well for three or four weeks, and then, in spite of rest and continuation of a high dosage of iodine, they began to go down hill, and all efforts to restore them to the original level of health ended in failure.

3 Clute, H. M., and Pilcher, L. S., Jr. Place of Iodine in Treatment of Goiter, *New England J. Med.* **210** 117, 1934.

4 Jackson, A. S., and Ewell, G. H. Danger of Prolonged Use of Lugol's Solution in Treatment of Exophthalmic Goiter with Case Reports and Study of Pathology, *Am. J. Surg.* **10** 475, 1930.

under 2 years of age and preferably for those under 1 year, it is best for those less than 6 months of age. Twenty-two children with subluxation and 11 with dislocation have been treated this way.

[**ED. NOTE.**—This method of therapy is simple, but unusual confidence must be placed in the mother or the attendant to assure satisfactory maintenance of the apparatus.]

*Status of Therapy for Congenital Dislocation of the Hip*—Lorenz<sup>2</sup> reviews the various methods of therapy—prophylactic, conservative, palliative and operative. He concludes that not one form should be proposed, but that each patient should be given what seems best in that case. A careful review of the literature is given, but few new recommendations of therapy are made.

[**ED. NOTE.**—This paper is of interest chiefly as a retrospect and final word of an outstanding authority on this problem.]

*Treatment for Congenital Clubfoot*—In an excellent article Kite<sup>3</sup> reviews the three essential elements of the deformity in congenital clubfoot: abduction of the forefoot, inversion of the os calcis and talipes equinus. He stresses the necessity of correcting these deformities singly in the aforementioned order if good results are to be obtained by conservative treatment. He has been able to correct severe deformity in 90 per cent of the cases without operative treatment and without forcible manipulation by the repeated application of plaster casts. He recommends the Hoke operation for clubfoot in the remaining 10 per cent of the cases when as much correction as possible has been obtained by casts and by wedging.

*Treatment for Clubhand*—Drinnenberg<sup>4</sup> reports his experience in the treatment of 3 children with clubhand, the result of a congenital defect of the radius. In 2 the ulna was transplanted into a wedge-shaped opening through the distal and the proximal row of carpal bones coming between the lesser multangular and the capitate carpal bones. After six weeks' fixation in plaster, exercises were begun. Position and function were reported to be good one year after operation. In the third case the second metacarpal bone was osteotomized and was put in apposition to the other fingers in order to form a thumb. Good function in the thumb was observed one year later.

*Congenital Absence of the Fibula*—Lapasset and Cahuzac<sup>5</sup> report in detail a case of bilateral absence of the fibula and review 295 similar cases reported in the literature. Their conclusions are that absence of the fibula is a fairly common congenital anomaly. The bone was

2 Lorenz, A. *Ztschr f orthop Chir* 63 93, 1935

3 Kite, J. H. *Surg, Gynec & Obst* 61 190, 1935

4 Drinnenberg, A. *Ztschr f orthop Chir* 63 297, 1935

5 Lapasset and Cahuzac. *Rev d'orthop* 22 110, 1935

not be available for the formation of thyroxine, and iodine would be stored in the thyroid. Davis' results are not definite, but he did demonstrate that the dog in which the pancreatic duct was ligated died much emaciated if it received iodides by mouth or di-iodotyrosine intravenously but would live indefinitely if given thyroxine intravenously. On the other hand, tyrosine given by mouth did not delay death. The iodine content of the thyroid glands of such dogs was great. Other studies, such as those of Zechel<sup>7</sup> and McEachern,<sup>8</sup> though providing nothing definite in regard to a twofold secretion of hormone by the thyroid gland, have notwithstanding added evidence that the substance used under the name thyroxine represents much more than the active properties of iodine.

When Dodds<sup>9</sup> in 1934 discussed substitutes for thyroxine, he brought out some interesting facts uncovered by chemists who are engaged in this search. Another compound isolated from the thyroid gland—3-5-di-iodothyronine—has been found capable of replacing thyroxine for therapeutic administration, showing, as Dodds put it, that "the thyroid lock may be picked by a skeleton key." He added "If we contrast the two formulae, it can be seen that they are relatively near to each other in structure, and all that is required is the introduction of two iodine atoms into the 3' 5' position." It is just these slight differences which should lead chemists eventually to the detection of the varying active principles, although there is probably a long road to be traveled before one comes to a clear field. But one should not be content to try to explain the action of iodine solely in terms of understanding of the action and composition of thyroxine. For though, as Dodds put it, "to many it would appear that the isolation of the hormone represents the be-all and end-all of the experimentalist's aim and object, yet we know that unless the actual mechanism of action is understood, we only understand one fraction of the problem."

It is not unreasonable to suppose that in estimating the chemical action of iodine administered as a preliminary to removal of the hyperplastic thyroid one is dealing with two distinct hormones. One of these may cause symptoms of thyrotoxicosis in the face of a normal or subnormal basal metabolic rate, appearing in conjunction with a so-called toxic adenoma or nodular thyroid.

<sup>7</sup> Zechel, G. Cellular Studies on Thyroid Gland, Surg., Gynec. & Obst. **54** 1, 1932.

<sup>8</sup> McEachern, D. Direct Measurements of Oxygen Consumption of Isolated, Beating Auricles from Normal and Thyrotoxic Guinea-Pigs, Bull. Johns Hopkins Hosp. **50** 287, 1932.

<sup>9</sup> Dodds, E. C. Hormones and Their Chemical Relations (Goulstonian Lecture), Lancet **1** 1048, 1934.

given intravenously. No untoward reaction followed intravenous therapy, in spite of the fact that the acid was not neutralized before injection. A single massive dose of cevitamic acid given either in pure form or as orange juice appears to favor healing of infantile scurvy as effectively as would the same total dose given in small daily portions over a period of eight days.

#### TUBERCULOSIS

*End-Results of the Treatment for Tuberculosis of the Spine*—Stalman<sup>8</sup> reviews the results of treatment in 218 patients suffering from tuberculosis of the spine, at Hanover, Germany. Gravitation abscesses were found in 23 per cent of the patients. Fistulas developed in 19 per cent. Paralysis was found in 14 per cent, but this symptom usually disappeared after rest in bed. Kyphos (persisting) was found in 89 per cent. The average period of healing was four and one-half years. Fifty patients had died (23 per cent), 5 from pulmonary tuberculosis, 7 of tuberculous meningitis and 5 of amyloid disease. The remainder had died of various diseases only secondarily related to tuberculosis. Treatment consisted of recumbency in a plaster bed with sun therapy and general measures to build up the patient constitutionally. The patient's progress was followed by roentgenographic studies and by the blood sedimentation tests. When the general condition was sufficiently improved and roentgenograms showed healing, the patient was allowed to be up, and a leather corset was worn. No operations were reported.

[ED NOTE—Stalman found the greatest number of cases in patients 2 years of age—an unfavorable reflection on the practice of public health measures in that community. No mention is made of recurrences, but the very high percentage of persisting deformity suggests that more vigorous corrective measures and possibly occasional spinal fusion might have prevented some deformity.]

*Tuberculosis of the Distal End of the Tibia and Fibula*—Logrosino<sup>9</sup> reports 5 cases of tuberculous involvement of the distal metaphysis of the tibia and fibula (4 of the former and 1 of the latter). This lesion unaccompanied by a synovial lesion of the ankle is very uncommon. Sinus formation is frequent. Absence of fever and only slight relative pain and increase of local heat are significant in differentiating this lesion from a pyogenic lesion. In only 1 case was the diagnosis proved. Treatment consisted of immobilization. Eventual recovery without loss of motion of the ankle occurred. It is of interest that in several of these cases there were multiple tuberculous lesions.

<sup>8</sup> Stalman, A. *Ztschr f orthop Chir* 63 319, 1935.

<sup>9</sup> Logrosino, D. *Chir d org di movimento* 19 545, 1935.

amount of normal thyroxine I dislike the term mild hyperthyroidism. No stage of hyperthyroidism should be looked on as mild. It is a grave condition calling for immediate consideration and treatment. Operation may not always be necessary, but to give the patient iodine medication (except for preoperative preparation) in the presence of demonstrable overactivity of the thyroid is a risky procedure.

#### FATALITIES

In urging operation in these cases of so-called mild hyperthyroidism, one must face the charge that death on the operating table has by no means ceased to take place. In a series of more than eight thousand thyroidectomies we have had five such deaths. One should never cease one's efforts to reduce this mortality to zero. Anything which one can contribute toward this, from experience, should be freely put at the disposal of one's colleagues, no matter how much one may feel personal responsibility in a particular case.

Of the five fatal cases in our series, one was an instance of a malignant condition of the thyroid. The immediate cause of death was an air embolism due to accidental tearing of an infiltrated jugular vein. In the four other cases the patient presented friable glands, and great traction was necessary. In the earlier cases I blamed the anesthetic for the fatal outcome and hoped to overcome the difficulty by using only nitrous oxide-oxygen anesthesia, with forced pressure when needed. This seemed to be satisfactory until recently, when another death occurred.

It seems possible that pressure on the carotid sinus or at least stimulation of the reflex in the sinus may account for the sudden stoppage of the heart which appears to be due to the anesthetic. Sigler,<sup>10</sup> in a study of the reflex in the carotid sinus made in 1933, found that there is a wide variation in the response of different persons to stimulation of this reflex. This he attributed to "variation in the vagotonic predisposition" which seems to be less in females and in persons with neurocirculatory asthenia. He also found that "local disease affecting the various components of the reflex vagal arc will lower the threshold of irritability of that arc, producing a heightened response." But as all the patients with similar disease conditions did not exhibit the same response, it was suggested to Sigler that "vagotonic predisposition is necessary in addition to the diseased state." This predisposition to slowing of the heart by pressure on the carotid sinus increases with age, reaching its maximum in middle life, and Sigler

<sup>10</sup> Sigler, L. H. Clinical Observations on Carotid Sinus Reflex Response to Carotid Sinus Pressure at Various Ages and Heart Rates and Rhythms, *Am J M Sc* 186 118 1933.



Fifty-five per cent of the patients were treated by amputation because they were seen in the late stages of the disease. Arthrodesis was done in only 11 cases. The diagnosis in 96 was verified by histologic section.

#### POLIOMYELITIS

*Some Factors in Control of Poliomyelitis*—Fairbrother<sup>13</sup> suggests that the sporadic nature of acute poliomyelitis in Great Britain is due to a wide dissemination of a virus of limited virulence which has imbued the majority of the adult population with some immunity. In handling these small outbreaks, he suggests that all patients with poliomyelitis and those suspected of having it should be isolated and that prophylactic inoculations of serum and gargles of oxidizing substances should be given to those who have come in contact with patients. Serum therapy by the intravenous and intramuscular routes should be instituted without delay in cases diagnosed in the early stages.

#### CHRONIC ARTHRITIS

*Osteo-Arthritis of the Hip Joints*—McMurray<sup>14</sup> analyzes a series of 89 cases of osteo-arthritis of the hip joint and concludes that while manipulation may produce relief from the symptoms and an increase of movement, these improvements are only temporary. With regard to operative procedures, he is of the opinion that although arthroplasty is ideal, usually no real benefit is secured for the patient, that arthrodesis of the hip is an extensive operation, and that while it removes the pain from the joint, it puts a great strain on the lumbar portion of the spine and the sacro-iliac region, which may become crippled later. The bifurcation operation of Lorenz, however, is simple, of short duration and, if correctly carried out, brings relief without loss of stability and puts no strain on the lumbar portion of the spine.

*Under-Water Gymnastics in Cases of Chronic Arthritis*—Currence<sup>15</sup> states that, regardless of type, patients suffering from chronic arthritis do not tolerate under-water therapy in a tank at the usual 86 F which is used in cases of poliomyelitis, and water at body temperature is required at the start, with a gradual increase to from 101 to 104 F depending on the point which produces maximal relaxation. The temperature is then gradually reduced to from 96 to 98 F, depending on individual comfort. Relaxation is characterized by vasodilatation of all of the capillaries of the skin. During treatment, the relaxation greatly relieves muscular spasm and pain. Joints which are painful on motion should be massaged by gentle stroking before active motion is

13 Fairbrother, R. W. *Brit M J* 1 916, 1935.

14 McMurray, T. P. *Brit J Surg* 22 716, 1935.

15 Currence, J. D. *Arch Phys Therap* 16 291, 1935.

# FIFTY-NINTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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## CONGENITAL DEFORMITIES

*New Treatment for Congenital Dislocation of the Hip*—Bauer<sup>1</sup> believes that congenital dislocation of the hip is due to an abnormal fixation of the fetus in utero. He substantiates this hypothesis by the finding of an asymmetry of the head associated with unilateral dislocations. As there has been a retardation in the development of the acetabulum and the head of the femur owing to the adduction of the legs in utero, the treatment consists of correcting and maintaining the legs in abduction in such a way that motion is still possible. A retentive apparatus is employed which is made of tape or ribbon in the following manner: (1) a pair of shoulder straps or suspenders is fastened to a circular band about the lower part of the chest and (2) ribbons are buttoned to the band, they extend posteriorly and are looped over the upper end of the tibia. In some instances the ribbons cross in the middle of the back. Motion is possible, yet abduction is maintained. Reduction occurs in from five to seven weeks. Retention in this position is continued for six months. The method is applicable for children

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This report of progress is compiled from a review of 173 papers selected from 313 titles relating to orthopedic surgery and appearing in medical literature approximately between July 1, 1935, and Oct 15, 1935. Only those which suggested progress were chosen for review.

<sup>1</sup> Bauer, F. *Chir d org di movimento* 19 539, 1935

and the muscles Fevre concludes that, except for the Achilles tendon, operation on tendons alone do not suffice but should be supplemented by neurotomy

"New Pathways for Children with Cerebral Palsy," by Rogers and Thomas,<sup>20</sup> a textbook which is the result of many years of experience in the treatment of cerebral palsy, is the best and most comprehensive treatise on this problem which we have seen. The authors not only discuss the physical rehabilitation but also give sane advice as to pedagogic procedures and the problems of social adjustment. A chapter by Dr. Nelson Hatt reviews the surgical procedures applicable to patients with cerebral palsy and their special indications. Many of the methods advocated have been worked out in a commonsense manner at the special camp, "Robin Hood's Barn," which is directed by the authors.

*Volkman's Paralysis*—Sorrel<sup>21</sup> advocates resection of both bones of the forearm in cases of Volkmann's paralysis. Enough bone is resected to allow complete extension of the fingers when the wrist is in extension. This sometimes necessitates removing as much as 4 or 5 cm of bone. The method of resection used is called *resection en chevron* and consists in making a slot in the end of one bone, into which is fitted the pointed end of the other bone. In addition to shortening the bone, it is necessary to strip the deep and superficial flexor muscles from their insertions and to cut or strip the pronator muscles.

[ED. NOTE—This suggests a rather formidable surgical procedure. The pushing distalward subperiosteally of the origin of the flexors of the forearm, as recommended by Steindler,<sup>22</sup> has in most cases produced sufficient relaxation of the flexor tendons and is a much simpler procedure.]

#### CIRCULATORY DISTURBANCES OF THE EXTREMITIES

*Thrombo-Anguitis Obliterans*—From experience with 48 cases of thrombo-anguitis obliterans in which sympathetic ganglionectomy was performed, Telford and Stopford<sup>23</sup> conclude that the operation not only is to be recommended, but is the only procedure that offers any hope of permanent relief. The disease is always bilateral, and the best results are obtained in younger men or in patients in whom the spasmodic element is well defined clinically, as evidenced by reaction to exercises and the customary preliminary vasodilator tests. With regard to positional color changes, it was found that the more clearly these were marked the less successful was the operation.

20 Rogers, Gladys G., and Thomas, Leach C. *New Pathways for Children with Cerebral Palsy*, New York, The Macmillan Company, 1935.

21 Sorrel, E. *Paris med* **1** 569, 1935.

22 Steindler, A. *Am J Orthop Surg* **15** 741, 1917.

23 Telford, E. D., and Stopford, J. S. *Brit M J* **1** 863, 1935.

entirely absent in two thirds of the cases. When only a part of the fibula was absent, the remaining portion was usually the upper or the lower third, but seldom the middle third, of the bone. Congenital absence of the fibula was rarely seen alone but was usually accompanied by other abnormalities. In the upper part of the leg the only changes noted were occasional slight exaggeration of the usual femoral curves and atrophy of the external femoral condyle. In the lower part of the leg the tibia was usually thickened and deformed, showing a marked bow at the junction of the middle and the lower third, this being concave on the side of the missing fibula. The tibia was rarely incomplete. In the foot multiple anomalies were found which were difficult to classify. These anomalies could not be grouped as belonging to either the tibial or the fibular segment of the foot. Various theories as to the cause of this condition were enumerated, but no conclusions were drawn. Treatment varied with each individual case, but in general conservatism was practical until late in or after the period of growth.

*Congenital Genu Recurvatum*—A case of congenital genu recurvatum is described by Middleton.<sup>6</sup> From the results of the clinical and histologic examinations he concludes that the deformity was due to contracture of the quadriceps extensor cruris muscle resulting from intra-uterine fibrofatty degeneration of the striated muscle fibers. The pathologic process was in all respects similar to that found in cases of arthrogryposis multiplex congenita, or, to use Middleton's term, myodystrophia deformans foetalis. Operative reduction was carried out in this case with a satisfactory result at the end of twenty-one months.

#### METABOLIC DISTURBANCES

*Cevitamic Acid Therapy in Cases of Scurvy*—Cevitamic acid, which has been synthesized from dextrose and assays of which revealed that 20 mg. of cevitamic acid is equivalent to from 15 to 20 cc. of lemon juice, was used by Goettsch<sup>7</sup> in treating 4 infants with severe scurvy long enough for comparison with control patients receiving orange juice. Serial roentgenograms and studies of excretions were made. Calcium was deposited in subperiosteal hematomas on the second, third, fourth and fifth days, respectively, while in the control infants who received orange juice calcification was not noted until the eighth, tenth and eleventh days. From the point of view of subjective symptoms, treatment with cevitamic acid resulted in satisfactory clinical improvement and was at least as effective as treatment with orange juice. In no infant was relief from pain obtained, even when a massive dose of 400 mg. of cevitamic acid was

<sup>6</sup> Middleton, D. S. Brit. J. Surg. 22: 696, 1935.

<sup>7</sup> Goettsch, E. Treatment of Infantile Scurvy with Cevitamic Acid, Am. J. Dis. Child. 49: 1441 (June) 1935.

The diagnosis is based on pain, swelling, elevation of the pulse rate, smears from the wound and blood cultures, discoloration, a bad odor, which is not a constant sign, elevation of temperature and the appearance of gas bubbles in the roentgenogram. Treatment is dependent on (1) accurate diagnosis, (2) early surgical intervention, involving multiple incisions into the skin and muscles if necessary (guillotine amputation well above the infected area being advocated in cases of extensive involvement of the muscles), (3) serum therapy (intravenously), and (4) dressings of a solution of hydrogen peroxide, a dilute solution of sodium hypochlorite or a solution of potassium permanganate, the chief point being not to pack the wounds too tightly.

#### NEOPLASMS

*Roentgenographic Diagnosis of Tumors of the Bone*—Geschickter<sup>27</sup> states that since there is a definite limitation to the findings in a lesion of the bone depicted by roentgenograms, it is important to obtain information from other sources to increase one's diagnostic ability. Limited to tumors of the bone, emphasis is given to roentgenographic features in this paper with remarks regarding treatment and whether or not roentgen therapy would be advisable in each case. Forty sets of excellent illustrations are given with accompanying photomicrographs in some cases. The lesions are divided into two groups: osteogenic tumors and tumors which are of nonosseous origin. In each instance a careful interpretation of each illustration is given. This is an excellent paper for summarizing the important tumors found by the roentgenologist or the orthopedic surgeon.

*Treatment of Giant Cell Tumors*—Geschickter<sup>28</sup> discusses the treatment of giant cell tumors under the headings of (1) indications for roentgen therapy and (2) indications for surgical intervention. He feels that four important factors should be considered before treatment is undertaken: (1) accurate diagnosis, (2) determination of the amount of healthy bone around the tumor, (3) the function of the bone involved, which may determine the type of treatment to employ, and (4) the possibility of performing a thorough surgical removal of the lesion without impairment of function. In a follow-up study of 300 cases in which various methods of treatment were used, the percentage of successful results was highest when resection was employed.

*Secondary Marble Bones*—Weber<sup>29</sup> suggests that the term "secondary marble bones" should be applied to the condition of widespread hyperplastic osteosclerosis which is sometimes seen in roentgenograms of the skeletons of patients suffering from carcinoma of the

27 Geschickter, C. F. *Am J Roentgenol* **34** 1, 1935.

28 Geschickter, C. F. *J Bone & Joint Surg* **17** 550, 1935.

29 Weber, F. P. *Lancet* **1** 377, 1935.

*Significance of Postnatal Development of the Tubular Bones for the Localization of Tuberculosis*—Stefko<sup>10</sup> states that the earliest changes in the bone of an infant in whom tuberculosis of the bone is developing secondary to a pulmonary lesion are to be seen about the tiny vessels which run in the canals of the lamellae. Perivascular infiltration is followed by erosion of the surrounding lamellae and rupture into the adjacent marrow cavities. At the age of 2 years vascularization of the lamellae is maximal. Also up to the age of 3 or 4 the marrow is of the myeloid type, which seems to favor the growth of tubercle bacilli. Older persons who chance to retain partially the myeloid type of bone marrow are particularly disposed to the development of tuberculous osteomyelitis. As a result of these infantile differences in bone, juxta-epiphyseal foci, which show only a poor tendency to calcify, remain quiescent on into later years. These foci may light up and later involve the marrow or the capsule.

*Traumatic Tuberculosis*—Schuller<sup>11</sup> reports 2 cases which he believes to be instances of traumatic tuberculosis. In both instances the process appeared in a local operative site in a child who showed no signs of local or general tuberculosis before operation and no evidence of general tuberculosis afterward. The first patient, a boy of 11 years, had a closed redressment done for a moderate grade, congenital hollow foot (bilateral). After removal of the corrective cast, in five weeks, a swelling was noted on the lateral aspect of the left foot. It was proved histologically to be tuberculous. In the second case tuberculosis followed an open reconstructive operation on a foot that had been deformed by infantile paralysis. A cast was worn for three months, when weight bearing was resumed. Seven weeks later, while the patient was still wearing the cast, pain developed. On the removal of the cast a swelling was seen on the lateral aspect of the foot. Its contents were proved to be tuberculous. A third case was recounted, although the patient was not seen personally.

*Association of Intrathoracic Lesions with Tuberculosis of the Bones and Joints*—Meng and Chen,<sup>12</sup> from a study of 100 cases of tuberculosis of the bones and joints in Chinese, found that 47 per cent of the patients had frank pulmonary involvement and 75 per cent had intrathoracic lesions of varying degree. According to the authors, the human tubercle bacillus was the invading organism more often than the bovine tubercle bacillus. Patients with lesion of a single joint had a greater preponderance of pulmonary involvement than did those with lesions of several joints. Of the 100 cases, draining sinuses were found in 66

10 Stefko, W. H. *Ztschr f Tuberk* 72 243, 1935

11 Schuller, J. *Munchen med Wchnschr* 82 834, 1935

12 Meng, C. H., and Chen, L. L. *J Bone & Joint Surg* 17 552, 1935

irrigate the joint with physiologic solution of sodium chloride for a half-hour or longer. The joint is then closed securely in layers and immobilized in a plaster cast. Favorable results were obtained in the cases reported. The methods of Willems,<sup>35</sup> i. e., early, adequate drainage followed by mobilization, and the method of Harris,<sup>36</sup> i. e., early drainage followed by immobilization in plaster, should, in the opinion of the author, be reserved for the cases which could not be handled by the joint-washing procedure. The frequency of acute trauma and distant foci of infection as causative factors in producing infection of a joint were emphasized.

*Treatment of Lymphedema by Plastic Operation*—Gillies and Fraser<sup>37</sup> report a case of lymphedema of both legs in which the condition resisted the usual forms of treatment. There was no evidence of, or history suggesting, acute lymphangitis. By thermal and excretion tests it was ascertained that the lymphatics of the limbs were patent and that the block lay at the junction of the extremities and the trunk. An almost perfect cure was established by transferring a long strip of skin and subcutaneous tissue from the forearm to the thigh and lateral abdominal wall. This "tap" had almost entirely removed the edema by the end of three months. Four operations were necessary to complete the "tap," but simpler methods were discussed.

*Shelf Stabilization of the Hip*—Howorth<sup>38</sup> found in a study of 61 hips which were congenitally dislocated that the shelf operation, which consists in turning out a bone flap from the ilium perpendicular with the horizontal axis of the body, was the most satisfactory type of operation. In this group about 75 per cent of the patients obtained good results. In the group in which the flap was turned upward the results were not as satisfactory. All results were rated from an anatomic, functional and symptomatic standpoint. The author is of the opinion that the shelf operation should not be done on a patient under 5 years of age. Early mobilization was indicated, but weight bearing was not permitted until the patient had good control over the hip or until the roentgenogram showed a well formed shelf. The operation was also done in 8 cases of infantile paralysis. Howorth does not advise correction of the anteversion of the femoral head, which was present in half of the cases, without reduction of the dislocation.

*Interinnomino-Abdominal (Hindquarter) Amputation*—Gordon-Taylor and Wiles<sup>39</sup> report 5 cases of interinnomino-abdominal amputation, in which 3 patients survived. They express the opinion that

35 Willems, C. Surg., Gynec. & Obst. **28** 546, 1919

36 Harris, R. I. J. Bone & Joint Surg. **7** 849, 1925

37 Gillies, H., and Fraser, F. R. Brit. M. J. **1** 96, 1935

38 Howorth, M. B. J. Bone & Joint Surg. **17** 945, 1935

39 Gordon-Taylor, G., and Wiles, P. Brit. J. Surg. **22** 671, 1935

permitted As muscle tone increases, active under-water exercise is permitted Maximum benefit results from regular, daily, systematic treatments Unless daily treatments are given, the tendency to retrogression during the interval is too great to allow noteworthy success Caution should be observed to avoid the complaint of fatigue following treatment Elderly persons suffering from osteo-arthritis have received the greatest benefit in the author's hands, but patients with rheumatoid arthritis whose disease has actually subsided and whose joints were not ankylosed can be helped also

#### THE KNEE

*Traumatic Injury to the Knee*—Darrach<sup>16</sup> studied 596 cases of traumatic injury to the knees seen at the Presbyterian Hospital in New York Of these, 157 were cases of internal derangement of the knee joint He favors a large exploratory incision and advocates a rigid aseptic nontouch technic

Spaulding,<sup>17</sup> summarizing his experience from operations in 146 cases of traumatic injury to the knee, discourages the use of large incisions He never uses a tourniquet In no case was there postoperative sepsis

*Injuries to the Cruciate Ligaments*—Milch<sup>18</sup> reports experiments and clinical evidence from which he concludes that, contrary to the general opinion, the anterior cruciate ligament is not a necessary structure and its loss is compatible with normal function of the knee joint He states that surgical efforts should be directed primarily toward repair of the internal lateral ligament by means of the Alwyn-Smith procedure rather than toward the repair of the cruciate ligament by the Hey Groves operation He reports a number of cases in detail to illustrate this thesis

#### SPASTIC AND ISCHEMIC PARALYSES

*Treatment for Spastic Paralysis*—Fevre<sup>19</sup> discusses the results of various therapeutic procedures in cases of spastic paraplegia The results are extremely variable, but surgical intervention is often indicated The author feels that is particularly true if the surgeon keeps in mind that improvement and not cure is the goal Most of the operations mentioned in Fevre's paper were performed on children with Little's disease Talipes equinus yields best to lengthening of the tendon Flexion deformity of the knee requires both lengthening of the tendon (or tenotomy) and neurotomy (Stoffel's operation) Adduction deformity of the thigh likewise requires operations on both the nerves

16 Darrach, W Ann Surg **102** 129, 1935

17 Spaulding, H V Ann Surg **102** 115, 1935

18 Milch, H Injuries to the Crucial Ligaments, Arch Surg **30** 805 (May) 1935

19 Fevre, M Rev d'orthop **22** 220, 1935



dislocation of the atlas on the axis may occur late, following a symptom-free interval. They stress the necessity of careful repeated roentgenographic study of fractures of the odontoid process and if evidence of progressive dislocation is obtained, fusion of the upper part of the cervical portion of the spine should be performed. If there is evidence of myelitis due to pressure, laminectomy should be performed before the fusion.

*Treatment and Prognosis in Fresh Dislocation of the Shoulder* — Biebl,<sup>43</sup> from Bolker's clinic in Vienna, reviews 110 cases of dislocation of the shoulder from two to eight years after injury. Forty-seven per cent of the dislocations were anterior, 52 per cent inferior and axillary and 1 per cent posterior. In the 60 patients with an axillary dislocation, 36 had a fracture of the greater tuberosity of the humerus and 7 showed paralysis. In persons under 42 years of age almost all dislocations were axillary. Function was normal in 83 per cent as a study of the end-results revealed. The most serious disturbances of function were found in persons over 40 years of age with an associated fracture of the greater tuberosity. Myositis ossificans was observed only after axillary dislocations. The fracture of the greater tuberosity healed in fairly good anatomic position in almost every case. Severe paralyzes continued in only 2 patients. Habitual and recurrent dislocations occurred only in the anterior type. There were 3 recurrent and 4 habitual dislocations. By early and satisfactory reposition and by long observation, the author concludes that in almost every case, even the severe ones, one could be assured of a satisfactory end-result.

[ED. NOTE — Biebl's group of axillary dislocations includes many that would be called anterior dislocations in American nomenclature.]

*Fractures of the Radius* — Magnus,<sup>44</sup> generalizing on the treatment for fractures of the radius, reports that in only 6 of 428 cases of fresh, typical fractures was open intervention required. A minimum of three weeks' fixation was found indispensable. Thereafter, the splint is removed daily for motion. He remarks that the results in patients from country insurance groups are inferior to those seen in the city hospital. The paucity of roentgenographic studies and the lack of accurate reduction was outstanding in the former group.

*Fractures of the Head and Neck of the Radius* — At the Massachusetts General Hospital, Jones<sup>45</sup> found that open reduction of a fracture of the head of the radius was attended in general by poor results. He concludes that open reduction and replacement should not

43 Biebl, R. Arch f Orth u Unfall-Chir **35** 381, 1935

44 Magnus, G. Munchen med Wchnschr **82** 1026, 1935

45 Jones, S. G. New England J Med **212** 914, 1935

# TETANUS AND GAS GANGRENE

*Analysis of One Hundred and Eighty-Five Cases of Tetanus*—After reviewing the reports of all cases of tetanus previously observed at the New Orleans Charity Hospital, Boyce and McFetridge<sup>24</sup> analyzed an additional 185 cases observed there from Jan 1, 1930 to Oct 31, 1934. They believe that in the average patient less than 50,000 units of antitoxin is inadequate while a dose of over 100,000 units is unnecessary and wasteful. Intramuscular injection alone gave a mortality of 49 per cent, when it was combined with an intravenous injection a mortality of 61 per cent was observed, and when it was combined with the local route of administration, the mortality fell to 33 per cent, though only 9 patients received this treatment. When intraspinal therapy was used the mortality was 66 per cent. This finding and other evidence led the authors to believe that intraspinal therapy should be discarded. During the past two years 15 patients were given tri-bromethanol in amylene hydrate to control spasm. The initial dose was from 80 to 100 mg per kilogram of body weight, with succeeding smaller doses before the effects of the previous dose had passed. Special attention was paid to functioning of the bowel and the bladder, to frequent aspiration of the secretion in the nasopharynx in deeply narcotized patients and to frequent changing of position to prevent hypostatic pneumonia. In this small series of patients the mortality was 23 per cent if the 2 patients who died six and twelve hours after admission are omitted.

*Treatment of Tetanus*—From the analysis of 21 cases of tetanus Cole and Spooner<sup>25</sup> suggest that the routine treatment for persons with this condition should be the intravenous injection of 200,000 units of antitoxin as early as possible and that this injection should be followed, after an interval, by a thorough cleaning of the wound, where bacteria are still active. The value of an adequate diet, of at least 2,000 calories per day, is emphasized. The administration of tri-bromethanol in amylene hydrate to control the spasms is recommended.

*Gas Gangrene and Gas Infections*—Ghormley,<sup>26</sup> from a study of 33 cases of gas infections at the Mayo Clinic, has arrived at certain conclusions and emphasizes two important factors in diagnosis and treatment. In this type of infection there are two distinct clinical pictures which are dependent on two separate types of organism: (1) *Clostridium welchii* or the gas bacillus, and (2) *Clostridium oedematis-maligni*, or *Vibrio septique*. Infection due to the latter is the more serious as to recovery and does not present the typical picture of gas gangrene.

<sup>24</sup> Boyce, F. F., and McFetridge, E. W. New Orleans M. & S. J. **87** 12, 1935.

<sup>25</sup> Cole, L., and Spooner, E. T. C. Quart. J. Med. **4** 295, 1935.

<sup>26</sup> Ghormley, R. K. J. Bone & Joint Surg. **17** 907, 1935.

*Fractures of the Femur at Birth*—Ryden<sup>48</sup> reports 13 cases of fracture of the femur at birth in which various methods of treatment were used. He found that reposition and maintenance of the reduced position of the fragments were always difficult. In many cases it was impossible and the fragments were left ununited in extreme malposition. Osseous union always occurred, and the malunion was eventually corrected by spontaneous remolding in from a few months to a year after union occurred. The children all learned to walk in the usual time. Examination of 6 patients after a lapse of from nine to twenty years revealed that the end-result was excellent in 5, whereas marked curvature at the site of the fracture was found in 1. A slight amount of shortening of the leg was observed in several cases. The author feels that the best method of treatment is extension in a portable plaster of paris bed, as recommended by Schanz.<sup>49</sup>

*Fractures of the Patella*—Campbell,<sup>50</sup> in a rather comprehensive paper, discusses the therapy of fractures of the patella. Of 127 cases, 74 were instances of complete transverse fractures, 64 of the fractures were recent, and 10 were ununited. The various surgical procedures are mentioned. The author stresses the importance of complete reduction of the fragments and fixation by a circular rustless steel wire, transfixing proximal and distal tendon fibers. Motion is advocated after the tenth day. The wire is removed later if necessary.

*Treatments of Fractures that Heal Slowly or Not at All*—Konig<sup>51</sup> found universally low basal metabolism rates in 9 persons with delayed union and pseudarthroses. He attributes delayed union to this cause. He lists the rates of 7 of the patients as from a minus 9 to 20 and of 2 as minus 23 and minus 29. He found that on the administration of a thyroglobulin preparation the basal metabolism rose and the fractures healed.

*Matti's Procedure of Implantation of Substantia Spongiosa in Cases of Fracture and Pseudarthrosis*—Konig,<sup>52</sup> on the basis of observations on 4 cases, recommends the method of Matti<sup>53</sup> for pseudarthrosis. After the ends of the fractured bone are freshened and the marrow cavity of the bone above and below exposed, the bones are approximated, and spongy bone is packed firmly about the operative site. The posterior fibrous attachments to the ends of the bone are not disturbed, according to the author. The periosteum is closed over the mass. Konig

48 Ryden, A. Surg., Gynec & Obst. 60 1098, 1935

49 Schanz, A. Prakt. Orthopaedie, Berlin, Julius Springer, 1928

50 Campbell, W. C. South. M. J. 28 401, 1935

51 Konig, F. Munchen med. Wchnschr. 82 86, 1935

52 Konig, F. Munchen med. Wchnschr. 82 860, 1935

53 Matti. Arch. f. orthop. Chir. 31 217, 1932

prostate These bones became infiltrated by millions of metastases, which are smaller than miliary, many consisting of only a few cells at the time of the patient's death Weber expresses the opinion that the growth of new bone is brought about by the action of the prostatic epithelium, which probably acts in the same way as transplanted epithelium of the urinary bladder or ureter

#### MISCELLANEOUS

*Diagnosis of Loose Bodies in the Elbow Joint*—Strasny<sup>30</sup> advises pneumography of the elbow joint as a means of visualizing free bodies and differentiating intra-articular from extra-articular bodies The puncture needle is inserted under local anesthesia laterally and posteriorly near the olecranon It is necessary to enter the joint with a single puncture, else the air or carbon dioxide injected thereafter may escape into the adjacent tissues

*Stenosing Tenosynovitis*—Soeur<sup>31</sup> reports 8 cases of stenosing tenosynovitis of the abductor and short extensor tendons of the thumb and gives an excellent summary of the pathologic picture and symptoms of the condition He is of the opinion that the condition is of traumatic origin and is best treated by open operation with division of the annular ligament and tendon sheath He considers conservative measures such as physical therapy and immobilization a waste of time in any but the mildest cases

*Staphylococcus Toxoid Clinical Trial*—Murray<sup>32</sup> suggests that the quantitative estimation of the staphylococcus antitoxin in the blood may be of diagnostic value in obscure conditions of the bone as he noted that while superficial staphylococcic infections influenced the quantity of antitoxin in the blood little if at all, staphylococcic infections of the bone increased it markedly The quantity of circulating antitoxin could be greatly increased by the injection of staphylococcus toxoid Four weekly injections of the toxoid, making a total of 0.75 cm., gave the maximum results The injections were accompanied by very few reactions

#### ORTHOPEDIC OPERATIONS

*Treatment of Acute Purulent Arthritis by Washing and Closure of the Joint*—Jones<sup>33</sup> feels that there is a certain type of septic joint, i. e., the intermediate, neither mild nor acute and fulminating, which responds well to the method of washing the joint advocated by Cotton<sup>34</sup> Eight cases are reported The method is to make an incision and thoroughly

30 Strasny, H Zentralbl f Chir **62** 1351, 1935

31 Soeur, R Rev d'orthop **22** 193, 1935

32 Murray, D S Lancet **1** 303, 1935

33 Jones, H T J Bone & Joint Surg **17** 559, 1935

34 Cotton, F J Boston M & S J **174** 779, 1916

bone from cartilage. He points out that the latter is less retarded by disease and disturbances of the endocrine system. The chief condition in which retardation of bone growth took place is infection at or near the epiphyseal line (tuberculosis), it is also caused by hypofunction of the pituitary gland, hypofunction of the gonads, hypofunction of the thyroid gland and deficiency of the parathyroid glands. Bone development is stimulated by hyperfunction of the anterior lobe of the pituitary gland and by periarterial sympathectomy. The method of bone repair is discussed, and the various theories as to this procedure are dealt with. Phemister is of the opinion that preservation of the periosteum is important in attempting to establish bone repair, and also that venous stasis plays a part in hastening bony union after fracture. Administration of calcium and phosphorus has not been shown to hasten the healing of fractures. Vitamin D has also been a disappointment as a factor in healing bone. The nature of ossification was discussed.

*Osteogenesis*—In a careful study of osteogenesis in young dogs, Bisgard<sup>59</sup> studied the repair of defects in the ribs at varying periods of time. He concludes that the costal periosteum is either directly or indirectly osteogenic and that the osteogenesis appears to take place in the cambium layer. If the periosteum was stripped of the cambium layer, it showed no osteogenic power.

He found that costal regeneration is limited by the periosteum and fails to take place if the periosteum is extirpated. He points out that various factors influenced osteogenesis. Among them are age, blood supply and the presence of a foreign body in intimate contact with the periosteum. He also noticed that thermal cauterization and chemical and electrical coagulation either retard or prevent osteogenesis.

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59 Bisgard, J. D. Osteogenesis. An Experimental Study, Arch Surg 30:748 (May) 1935.

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#### REPRINTS OF MacCOLLUM'S ARTICLE OBTAINABLE

Requests addressed to Dr. Donald W. MacCollum of Boston for reprints of his article, entitled "Chemical Study of the Spermatogenesis of Undescended Testicles," which appeared in the August issue of the ARCHIVES OF SURGERY, were destroyed, through inadvertence, during his absence. If those who wrote for reprints will address him again, at 81, Wimpole Street, London, W 1, England, they will receive the pamphlet.

although this must remain one of the most colossal operations in surgery, with organization of team-work and the perfection of transfusion arrangements the mortality should be brought still lower. An excellent description of the operation is given.

*Operation for Bunion*—McBride<sup>40</sup> reports an operative procedure for the treatment of bunion. This method consists in exposure of the metatarsal phalangeal joint through a 2 inch (5 cm) incision beginning in the web between the first and the second toe and extending posteriorly parallel to the tendon of the extensor hallucis longus muscle. The conjoined tendon of the adductor hallucis and the flexor hallucis brevis muscle is exposed on the medial aspect of the base of the phalanx and its insertion divided. The external sesamoid bone is excised by sharp dissection, except when the operation is done on a person under 30 years of age, in which case the bone is left intact. The conjoined tendon is transposed and reattached subperiosteally to the lateral aspect of the first metatarsal bone just behind the joint line. The bursa and capsule are shortened sufficiently so that when they are resutured the toe is held in the corrected position. The medial aspect of the head of the metatarsal bone is exposed, and the exostosis is removed with a thin osteotome, care being taken not to injure the inferior weight-bearing area or the cartilaginous surface of the joint. The wound is closed in the usual fashion, the toes being held in the corrected position by short plaster boots. Weight bearing is begun two weeks after operation with the toe held in the corrected position by means of adhesive tape for three or four weeks after operation. The author reviews 39 consecutive cases with excellent results, both from the point of view of the patient and from that of the surgeon. Overcorrection of the deformity was obtained in 2 cases.

#### TRACTURES AND DISLOCATIONS

*Atlanto-Axial Dislocation Unassociated with Trauma*—An excellent review of the literature relative to atlanto-axial dislocation unassociated with trauma is given by Hess, Bronstein and Abelson<sup>41</sup> with a discussion of the various conflicting opinions on the mechanism of the production of this lesion. The authors add 2 more cases to the 22 previously reported and discuss several factors which may explain the production of such a lesion.

*Progressive Atlanto-Axial Dislocation*—Kahn and Yglesias<sup>42</sup> point out that after fracture of the odontoid process progressive

<sup>40</sup> McBride, E. D. Conservative Operation for "Bunions," J A M A 105 1164 (Oct 12) 1935

<sup>41</sup> Hess, J. H., Bronstein, I. P., and Abelson, S. M. Atlanto-Axial Dislocations, Am J Dis Child 49 1137 (May) 1935

<sup>42</sup> Kahn, E. A. and Yglesias, L. Progressive Atlanto-Axial Dislocation, J A M A 105 348 (Aug 3) 1935

southern states have mentioned the greater resistance of Negroes in general to bullet wounds. But, as already stated, the absence from such records as now remain of information as to the number of Negro patients who recovered ends any further discussion of this matter. It is of interest, however, to know that tissues in the bodies of Negroes are more compactly knit together than those in the bodies of white persons and that in the postmortem examinations of the bodies of Negroes sharp knives are more quickly dulled.

#### STAGES IN THE DEVELOPMENT OF MODERN METHODS OF TREATMENT

A number of excellent accounts of the evolution of therapy of bullet wounds of the abdomen have been written.<sup>2</sup>

There was a long period before the discovery of anesthetics and antiseptic methods during which surgical procedures were inadequate. But there were many far-sighted surgeons during that time, especially those with military experience, who recognized that an ideal treatment would consist in opening the abdomen and repairing the injuries. Hamilton<sup>3</sup> carried this period back to statements made by Wiseman<sup>4</sup> in 1676, and the opinion of Wiseman was referred to in a later comment on the practice of treating gunshot wounds by surgical intervention.<sup>5</sup> But the subject was evidently not new then, as is apparent from the following quaint quotation by Otis<sup>6</sup> of advice given by Jherome of Bruynswyke,<sup>7</sup> who said in 1525

Whan the guttes is wounded ouertwhart or is in pecis, than it is dedly, & if it be lengthe woundyd, it may be holpen. If that the wounde of the belly is not grete

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2 (a) Otis, G. A. *Injuries of the Abdomen, in Medical and Surgical History of the War of the Rebellion*, Washington, D. C., Government Printing Office, 1877, part 2, vol 2, chap 6, p 1. (b) Barnard, J. H. *Des plaies de l'intestin par armes a feu*, These de Paris, no 263, Paris, A. Davy et Fils Aine, 1887, p 79. (c) Nimier, H. *Sur la seméiologie et le traitement des coups de feu de l'abdomen par petits projectiles*, Arch gen de med 21 207, 1888. (d) Verchere, F. *Des plaies de l'intestin par armes a feu de petit calibre*, Rev gen d sc med 32 297, 1888. (e) Amat, C. *Essai critique et clinique sur le traitement des lesions traumatiques de l'abdomen par projectiles de petit calibre*, Gaz med de Paris 1 121, 1892. (f) Klemm, P. *Pathologie und Therapie der Schussverletzungen des Magens und Darms*, Samml klin Vortr no 142, 1896 (Chir no 39, p 321).

3 Hamilton, J. B. *Penetrating Pistol Shot Wound of Abdomen, Laparotomy, Suture of Intestine, Pelvic Hematoma, Recovery*, J A M A 5 202 (Aug 22) 1885.

4 Wiseman, R. *Severall Chirurgicall Treatises*, London, R. Royston, 1676.

5 *Laparotomy in Gun-Shot Wounds of the Abdomen*, editorial, J A M A 12 54 (Jan 12) 1889.

6 Otis, 2<sup>a</sup> p 116.

7 Brunschwig, H. *The Noble Experyence of the Vertuous Handy Warke of Surgeri, practysyd and compyled by the moost experte mayster Therome of Bruynswyke*, London, Peter Treverus, 1525.

be attempted except in cases of epiphyseal separation and occasionally in a case of fracture of the neck of the radius. Excision of a single small fragment which did not articulate with the ulna was attended by good results. He concludes that in all cases of comminuted and displaced fracture of the head and neck resection of the head should be performed within the first two weeks after injury. He points out that ossifying hematoma or myositis is a common complication. He employs the posterior lateral approach for removal of the head of the radius and the anterior approach for replacement of dislocations of the head of the radius.

*Fractures of the Neck of the Femur*—In an excellent paper, Bunnell<sup>46</sup> discusses the entire subject of fracture of the neck of the femur, blood supply, physiology of healing and methods of fixation. In conclusion, he feels that internal fixation is desirable, by multiple pinning, the Smith-Petersen nail or the Albee bone graft. Satisfactory reduction must precede fixation. Although the author prefers autogenous bone grafts, these in turn transfixed with smaller grafts, he believes that metal fixation is satisfactory if accurately done. To overcome or to facilitate blind nailing, he has devised an instrument with two sights. Whatever manner of fixation is used, weight bearing must be postponed at least six months, until the head of the femur has recovered from the primary injury or recalcified following the secondary changes seen so frequently.

In the study of monographic proportions Pauwels<sup>47</sup> considers fractures of the femoral neck from the point of view of mechanics. He divides these fractures into three grades. In the first grade are those in which the angle of fracture is not more than 30 degrees from the horizontal. In the second grade are those in which the fracture lies between 30 and 50 degrees from the horizontal. In the third grade are those in which the fracture lies more than 50 degrees from the horizontal. The author has studied these three groups in relation to muscle-pull and weight-thrust and the influence of these factors on healing. Prognosis can be given according to the mechanical position of the fracture, not its position on the neck of the femur. In type 1, bony union usually follows almost any therapy. In type 2, the prognosis must be guarded, in type 3, it is usually poor. In type 2 more exact fixation of the fragments is indicated, and nail or screw fixation is often helpful. For type 3 the fracture must be changed into a type 1 fracture, for which the author advises the osteotomy of Weil, a subtrochanteric wedge-osteotomy which later makes a more direct downward pressure on the femoral neck. The author reports illustrative cases. A careful analysis of the mechanics of the hip joint is given.

<sup>46</sup> Bunnell, S. California & West Med 43 27, 1935

<sup>47</sup> Pauwels, E. F. Ztschr f orthop Chir 63 1, 1935



have contended that this operation by Kinloch, performed seven months after the patient was shot, was done to repair a preternatural anus and was not a laparotomy

The second period began with the demonstration that the abdomen may be opened widely with safety in order to search for and treat by surgical methods disease which it may contain. The declaration by Sims<sup>9</sup> in 1882, so often cited, that laparotomy for bullet wounds is as feasible as that for ovariectomy may have aided in making the procedure popular. But it should be remembered that when endorsement of such measures began, in about 1885, abdominal section for a great variety of diseases, mainly those of the female pelvic organs, had been widely practiced for some time. It had also been in vogue for the treatment of injuries of the abdominal organs due to causes other than firearms. Morton<sup>13</sup> credits Walter,<sup>14</sup> a well trained German surgeon who came to America at the suggestion of the surgeon Dieffenbach, with having performed the first laparotomy for intra-abdominal injury. The operation, which was successful, was done at Pittsburgh in 1859. Walter said "Recovery from an injury of such a formidable character as rupture of the bladder with extravasation of urine into the abdominal cavity has not, as far as we know, ever been obtained by the ordinary means of practice." He insisted that his procedure was "not only legal but imperative." When Morton<sup>13</sup> made his first survey he found published or other information available about twenty laparotomies for stab wounds, nine for ruptured bladder and eight for lacerations of the bowel by blunt force. In view of the progress in abdominal surgery which had been made, it seems surprising that prompt laparotomy for bullet wounds of the abdomen was not advocated earlier.

This second period was brief, perhaps a decade or two. Ultimately a policy of prompt operation was fully sanctioned. But this required time, and for a number of years disputes in medical societies were quite general. Some surgeons were outspoken in expressing preference for noninterference, others were in favor of immediate laparotomy, and a third group advocated operation when certain symptoms appeared.<sup>15</sup> Amat<sup>2e</sup> enumerated twenty different meetings of the French society of surgery in Paris held from 1886 to 1891, at which these subjects were

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13 Morton, T S K. Abdominal Section for Traumatism, with Reports of Five Cases, *J A M A* 8 225 (Feb 26) 1887

14 Walter, A G. A Case of Rupture of the Bladder Treated by Abdominal Section, *M & S Reporter*, Phila 7 153, 1861

15 The surgical treatment of acute appendicitis underwent a similar evolution before surgical intervention followed the diagnosis as a routine as is the case at present, and controversies now prevail as to when removal of the acutely inflamed gallbladder is indicated

comments especially on the rapidity of callus formation in 3 of his cases. The spongy bone is obtained readily from the greater trochanter of the femur in considerable quantities.

#### RESEARCH

*Mycotic Lesions in Experimental Animals*—Sostegni<sup>54</sup> introduced several of the myces in saline suspension into the medullary canals in one series on rabbits and into the joints in a second series. Photomicrographs are shown of the lesions. Considerable discussion of the changes in the joints and bones is given, but no roentgenograms.

*Size of the Virus of Poliomyelitis*—From an analysis by means of fractional ultrafiltration of broth suspensions of the enlargements of spinal cords of monkeys dying of poliomyelitis, Elford, Galloway and Perdrau<sup>55</sup> conclude that the virus of acute poliomyelitis varies from 8 to 12 millimicrons in diameter.

*Anatomic Observations of Senile Changes in the Shoulder*—Keyes,<sup>56</sup> from a study of 192 shoulders in cadavers from the dissecting room, found that the most common abnormality was a partial rupture of the supraspinatus tendon, others were hypertrophic changes of greater tuberosity, calcification of the supraspinatus tendon, adhesions in the subacromial bursa, erosion of the floor of the subacromial bursa, fragility of the greater tuberosity and erosion of the articular surface of the head of the humerus. These changes are ascribed to age and are considered degenerative rather than due to infection. In every case the biceps tendon was intact, and there were no complete ruptures of the supraspinatus tendon.

*Rupture of Intervertebral Disk in Experimental Animals*—Experimental rupture of the nucleus pulposus of rabbits performed by incision is reported by Filippi.<sup>57</sup> At ten, twenty, forty, eighty and one hundred days the animals were killed, and the intervertebral disks were studied. The fibrocartilage was not healed until forty days, and at this time passive motion was limited. At eighty and one hundred days the lesion in the fibrocartilage was healed, the area of the nucleus pulposus was replaced with quite elastic fibrocartilage and the passive motion of the joint was only slightly limited. The nucleus pulposus did not regenerate at any time.

*Bone Growth and Repair*—Phemister<sup>58</sup> discusses the methods of bone growth by calcification in fibrous tissue and the development of

<sup>54</sup> Sostegni, A. *Chir d org di movimento* **21** 107 1935

<sup>55</sup> Elford, W. J., Galloway, I. A., and Perdrau, J. R. *J Path & Bact* **40** 135, 1935

<sup>56</sup> Keyes, E. L. *J Bone & Joint Surg* **17** 953 1935

<sup>57</sup> Filippi, A. *Chir d org di movimento* **21** 1 1935

<sup>58</sup> Phemister, D. B. *Ann Surg* **102** 261 1935

thirty-two cases because MacCormac in the reprints of his oration added reports of two more laparotomies to that of the thirty he first collected<sup>22</sup> To these Barker added reports of twenty-six

TABLE 1—*Early Statistics*

Author	Year	Total	Deaths	Mortality (Percent age)	Comment
Morton, T S K Abdominal Section for Traumatism, Proc Philadelphia Co M Soc S 11, 1888 (read before the Society Jan 26, 1887), Abdominal Section for Traumatism with Reports of Five Cases and Tables of All Recorded Cases, M News 70 215, 1887, footnote 1 <sup>3</sup>	1887	22	17	77.2	16 of the 22 laparotomies were performed by American surgeons
Barnard <sup>b</sup>	1887	24	18	75.0	Laparotomies were performed as follows in 1882, 2 in 1883, 1 in 1885, 6, in 1886, 12, in 1887, 3
MacCormac <sup>19</sup>	1887	30	22	73.3	Morton's list of 22 is included
Carson, A B Injuries of the Abdomen and Their Proper Treatment, J A M A 9 577 (Nov 5) 1887	1887	44	30	68.4	MacCormac's table is included
Chauvel, J De la conduite à suivre dans les blessures par coup de feu des cavités viscérales, Cong franc de chir Proc verb 3 55, 1888	1888	41	29	70.7	All but 3 cases listed in MacCormac's table are included in these 3 débridement operations
Coley <sup>20</sup>	1888	74	44	59.4	Of patients having laparotomies in the first 12 hrs, 17 recovered and 22 died
Dalton, H C Gunshot Wound of the Stomach and Liver Treated by Laparotomy and Suture of Visceral Wounds with Recovery, Ann Surg S 81, 1888	1888	69	41	59.4	MacCormac's list is included
Barker, J E J <sup>21</sup>	1888	58	35	60.3	MacCormac's list is included
Morton, T S K Abdominal Section for Traumatism with Tables of Two Hundred and Thirty Four Cases, J A M A 14 1 (Jan 4) 1890	1890	110	74	67.2	Sixty eight American surgeons operated on 94 patients, 16 foreign surgeons operated on the remaining 16
Korte <sup>23</sup>	1890	64	42	65.6	Korte does not give a table, his material was derived mainly from American literature
Martin and Hare <sup>10</sup>	1891	130	86	66.2	Several "débridement" operations are included
Coley W B The Treatment of Penetrating Gunshot Wounds of the Abdomen, with an Analysis of One Hundred and Sixty Five Cases Treated by Laparotomy, Am J M Sc 101 243, 1891	1891	165	111	67.0	This article includes a number of operations not mentioned in the literature
Luhe Zur Behandlung durchbohrender Bauchwunden, Deutsche mil arztl Ztschr 21 147, 204 and 233, 1892	1892	152	95	62.5	The mortality (53 deaths) for 92 patients whose laparotomies were performed during the first 12 hrs was 57.4%
Conner <sup>20</sup>	1893	188	127	67.5	Fifty five American surgeons performed 174 laparotomies, there were 123 deaths

The title of Korte's article<sup>23</sup> intimates that his material was possibly derived from surgical experience in time of war, but it was obtained chiefly from American literature MacCormac<sup>19</sup> said that gunshot

<sup>22</sup> There are only thirty in the translation into German of his oration (Samml klin Vortr no 316, 1888 [Chir no 99, p 3025])

<sup>23</sup> Korte, W Die Kriegschirurgische Bedeutung und Behandlung der Bauchschüsse, Berl klin Wchnschr 27 72, 1890

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## PEACE TIME BULLET WOUNDS OF THE ABDOMEN

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AND

E R LE COUNT, M D†

CHICAGO

This study, begun a number of years ago,<sup>1</sup> deals with the results of treatment in the Cook County Hospital, Chicago, of patients with bullet wounds of the abdomen (table 3) during the period from 1911 to 1924, when one of us (E R L) made postmortem examinations in the morgue of that hospital for the coroner of Cook County. Although a decade has passed, it seems desirable to record these results. The number of patients, 343, is large, opportunity is given to compare the surgical work done in the period covered with that performed in the same hospital during subsequent years, the number of recoveries may be contrasted with those attained in other places, and, finally, because the theme is "peace time wounds" sustained in civil life, additional information is made available for reviewing the numerous differences between such wounds and wounds of the abdomen caused by missiles used in war.

The 343 patients who form the basis of this report were among a total of 432,293 patients admitted to the Cook County Hospital during the period covered by this study—a ratio of 1 to 1,260. During the year 1924 and during the period from 1911 to 1918, the only years available for comparison in our study, the ratio of patients entering the Cook County Hospital with bullet wounds of the abdomen was 1 to 1,692, whereas during the five years immediately following the World War, the ratio was 1 to 882. This disregard for human life exhibited during the years immediately following the war has been widely discussed.

Information as to the number of Negro patients in our series was obtained only from the records of the number of patients (205) who died and were examined at autopsy, this is not quite an adequate basis from which to draw conclusions. Of the 205 patients, 149 were white, 54 were Negroes and 2 were Mexicans. A number of surgeons in the

† Dr E R Le Count died on Aug 23, 1935.

From the Norman Bridge Pathological Laboratory and the Surgical Department of Rush Medical College of the University of Chicago.

<sup>1</sup> Dr W M Moncrief, Dr Chester Guy, and Dr G J Rukstina assisted in examining some of the clinical records.

TABLE 2—Reports by Single Surgeons and From Particular Hospitals

References	Number of Necropsies	Mortality (Percent)	Comments
Barrow, D. Four Cases of Gunshot Wound of the Abdomen Treated by Laparotomy, with Remarks, <i>J. A. M. A.</i> 12, 833 (June 15) 1890, Gunshot Wounds of the Abdomen with Cases, <i>ibid.</i> 15, 203 (Aug. 9) 1890. Barrow, D. W. Gunshot Wounds of the Abdomen, Kentucky <i>V. J.</i> 16, 243, 1918.	19	26.8	D Barrow and D W Barrow, father and son, worked at Lexington, Ky 13 patients, 4 of the 6 and only 1 of the 13 died, 13 were Negroes, 6 were white persons. Injury operation interval was for 1 patient 13 hrs, for the 18 remaining 6 hrs or less, for many less than 3 hrs. One patient recovered after D W Barrow repaired 17 perforations and resected parts of both colon and small bowel.
von Bramann. Zur Behandlung der Schusswunden des Dunndarms und Mesenteriums mit Krankenvorstellung, Verhandl d. deutsch. Gesellsch. f. Chir., 1889, p. 118. Wlemuth. Die Behandlung der Schussverletzungen, <i>Arch. f. klin. Chir.</i> 60, 492, 1900. Loening, K. Die Behandlung der Schussverletzungen des Abdomens, Inaug. Dissert., Halle on Saale, Kaemmerer & Co. 1902. Stieda. Ueber Schussverletzungen des Abdomens, Muenchen med. Wchenschr. 53, 673, 1906.	12	50.0	12 patients, 6 deaths. 1 patient whose injuries were reported by von Bramann recovered. Wlemuth reported 7 cases with 3 recoveries (the cases of 6 of the 7 presented by von Bramann to the German Surgical Society, 1893, were never published). Loening reported 3 cases with 1 recovery. Stieda reported 1 recovery. The average injury operation interval for those recovering was 6 hours, to those dying 21.3 hrs. of 7 patients having injuries to a single viscus, 3 recovered, of 5 having injuries of two or more viscera, 3 recovered.
Korte, W. Über die Chirurgie der Gallenwege und der Leber, Samml. klin. Vortr. n. f. no. 40. ( <i>Chir.</i> no. 12, p. 243), 1892. von Haselberg, A. Zur Casuistik der Schussverletzungen im Frieden, Inaug. Dissert., Berlin, G. Schade, 1893. Kroner, M. Erfahrung über Friedensschussverletzungen, <i>Arch. f. klin. Chir.</i> 73, 648, 1905.	15	66.6	From Korte's urban clinic, Berlin, Germany, from 1890 to 1893 inclusive korts had 3 cases with 1 death. Haselberg, 3 with 3 deaths, and Kroner, 9 with 6 deaths. of 15 patients operated on by different surgeons 10 died. One patient with no visceral injury recovered, of 3 with injury to a single organ 2 recovered, and of 11 with injury to 2 or more organs only 2 recovered. Average injury operation interval, 7 hrs.
Miles, A. B. Gunshot Wounds of the Intestines. Clinical Report of Thirteen Cases. Remarks on Diagnosis and Treatment, <i>Tr. Am. S. A.</i> 11, 337, 1893.	23	20.0	Reports from the St. Louis City Hospital, St. Louis, from 1892 to 1895 20 males and 3 females. Average injury operation interval for 20 patients, 4.33 hrs., for 3 not stated. Six deaths. In 7 patients the small bowel alone was injured, in 1 it was injured together with other organs, the stomach alone was injured in 1, it was injured along with other organs in 6, the colon alone was wounded in 2. From the Charity Hospital, New Orleans 7 were Negroes, 5 were white persons. Nine patients died, 4 recovered. One white man recovered after 16 perforations of the bowel were repaired, 1 who died had 20 perforations of the bowel from shotgun missiles. From the Maryland University Hospital Clinic (from 1896 to 1916) R. Winslow dealt with the wounds of 23 patients, there were 5 deaths in his series. N. Winslow in 1922 treated 21 patients, 13 died. Summarized data for the 34 patients are as follows: 18 deaths and 10 recoveries. 14 white persons, 18 Negroes and 2 whose race was not stated. 27 males, 6 females and 1 whose sex was not stated, the youngest was 3 yrs., 17 died of wounds of hollow viscera. 1 who recovered had 14 perforations of the small bowel with bird shot, the injury operation interval in most cases was less than 4 hrs., bullet wounds of the duodenum in 1 body and of the colon in 2 others were discovered post mortem.
Winslow, R. Gunshot Cases, Maryland <i>M. J.</i> 34, 314, 1895. 1896, in New Orleans <i>M. &amp; S. J.</i> 23, 463, 1895-1896. Gunshot Wounds of the Peritoneal Cavity and Contained Viscern South <i>M. Rec.</i> 26, 129, 1896, Report of Eight Cases of Penetrating Gunshot Wounds of the Abdomen, with Injury to the Hollow Viscera, <i>Ann. Surg.</i> 28, 487, 1898. Fene 1914 Gunshot Wounds of the Abdomen, <i>J. A. M. A.</i> 6, 1165 (Oct. 3) 1914. Gunshot Wounds of the Intestines, Bull. Univ. Mary land School of Med. 66, 1916. Winslow, N. Penetrating Abdominal Wounds, <i>Surg. Gynec. &amp; Obst.</i> 34, 617, 1922.	34	52.9	From the Charity Hospital in New Orleans. Seven patients died, 6 recovered one of the 1 Negroes, a boy, aged 15 recovered after 11 perforations were repaired, 12 underwent operations shortly after injury, 1 who died had a second laparotomy.
Parker, W. I. Bullet Wounds of the Abdomen. <i>Tr. South S. &amp; Gynec. A.</i> 9, 272, 1896.	13	33.8	

nowgh, than shall ye make it greater as I shall shewe you hereafter, than shall you take out proply the guttes, and sow it thereafter as it is needful with a skynners nedyll Jamericus, Theodoricus, Rogerius lay elder pypes in the guttes under the seme, that the same rotte not Wilhelmus and some other, lay there in a part of a cryer of a throte goll of a beest, as the IV maysters sayth But Lanfrancus and Guido they thinke it not be profytable, for that nature is inclnyed to outdrawynge strange thyngys, and thus yt helpt not therefore it was layd, and it is better that the guttes be sowyd, as afore is sayd, and that it be clenysyd of the unclenes

Presumably similar opinions prevailed with regard to abdominal wounds before the days of firearms

Many of these earlier surgeons did enlarge the wounds due to firearms and repair injuries apparent *de visu et de tactu* Bainard<sup>2b</sup> mentioned twelve surgeons, beginning with Lairey in 1779, who treated wounds of the bowel in this manner They did not perform laparotomies, abdomens were not opened freely and explored<sup>8</sup> Bainard<sup>2b</sup> omitted from his list of twelve surgeons the name of Newell of New Brunswick, N J, who told Sims<sup>9</sup> that he (Newell) had made "an incision 1½ inches above the crest of the ileum and removed a gun wad, composed of tow, paper, shot, a printer's type, and a piece of a man's vest—in all, sufficient to fill a tumbler half full" Recovery followed This Newell did in 1847, the day after the shooting His operation is included in MacCormac's table as a laparotomy, but the date of its execution was erroneously given by MacCormac as 1882, the year in which Sims announced that Newell had told him Mention of Newell's operation is omitted from the list of laparotomies in the monograph by Martin and Hare<sup>10</sup> Newell's patient had accidentally shot himself with a shotgun Sims said "Dr Newell did, thirty-four years ago, what I now advise to be done in all cases of shot-wounds of the abdominal cavity" This is of interest solely with reference to who made the first laparotomy for bullet wounds Kinloch<sup>11</sup> claimed he should be given the credit for this for an operation he performed on May 27, 1863 Others,<sup>12</sup> however,

8 In some of the tables on laparotomies published subsequently, a few of these "debridement" operations are wrongly included, notably two by Baudens in 1830 and 1831, respectively, as stated by Otis,<sup>2a</sup> (p 125) and by A B Graham, (Gunshot Wounds of the Abdomen, Indiana M J 20 413, 1902), and one by Sevastopoulo as stated by Reclus (Bull et mem Soc de chirurgiens de Paris 15 132, 1889)

9 Sims, J Marion Remarks on the Treatment of Gunshot-Wounds of the Abdomen in Relation to Modern Peritoneal Surgery, Brit M J 1 184 1882

10 Martin, E, and Hare, H A The Surgical Treatment of Wounds and Obstruction of the Intestines, Philadelphia, W B Saunders Company, 1891

11 Kinloch, R A Pistol-Shot Wound of the Abdomen Treated by Laparotomy and Suturing the Intestines, Tr Am S A 5 183, 1887

12 Stimson L A On Gunshot Wounds of the Abdomen with Especial Reference to Wounds of the Intestines, New York M J 50 449, 1889

TABLE 2—*Reports by Single Surgeons and from Particular Hospitals—Continued*

References	Number of Patients	Age	Mortality (Percent)	Comment
Brown, J Y Penetrating and Perforating Gunshot and Stab Wounds of the Abdomen with Reports of Cases, Ann J Obst 48 707, 1903, New York M J 70 723, 1904, Report of Case, Penetrating Gunshot Wound of the Abdomen, Louisville Month J M & Surg 11 340, 1904 1905 St Louis M Rev 51 254, 1905	10	2	50.0	From the City Hospital, St Louis Each of the 2 articles appeared in 2 different journals. Observations on 10 patients are discussed. There were 8 male and 2 female patients, 5 of the male, and none of the female patients died. For 7 the injury operation interval was short 4 of the 5 who died had resections of the bowel the other who died had a bleeding wound of the liver, an overlooked wound of the cecum was found post mortem in 1 body.
Ossig Zur Pathologie und Therapie der Revolver-schussverletzungen des Kopfes und Rumpfes, Beitr 7 klin Chir 17 511, 1903 Letzte Magenschnus, Centralbl f Chir 36 112, 1909 Seheyer K Ueber Nierenschussverletzungen, Klin Wochenschr 1 1463, 1909	10	2	60.0	From Tietze's surgical clinic at Allerheiligen Hospital in Breslau, Germany. A total of 10 cases with 6 deaths are reported. Ossig had 3 with 4 deaths Tietze 3 with no deaths, Seheyer had 2 with 2 deaths. Of 5 patients with injury to a single organ, only 1 died all with injuries to 2 or more organs. In 1 body a wound of the stomach, and in another an extraperitoneal wound of the urinary bladder were overlooked. The injury operation interval is stated for 2 patients only for 1 it is given as "prompt," for the other as "a few hours."
Gebele, H Ueber penetrierende Bauchstich und Schusswunden, Munchen med Wochenschr 50 1417, 1903	15	None mentioned	46.7	From Angerer's surgical clinic in Munich, Germany, from 1897 to 1902. Seven of the 15 patients reported on died.
Harris, M L On the Treatment of Penetrating Wounds of the Abdomen, Ann Surg 19 350, 1904	10	3	70.0	From various hospitals in Chicago. Three of 10 patients died. In 1 body there were found after death 2 holes in the stomach and 1 wound of the diaphragm which had been unsuspected at the time of the operation. The injury operation interval was 3 hrs or less, in 2 patients who recovered no viscous was injured.
Opel, W A Uncomplicated Compound Gunshot Wounds of the Stomach Russk vrach 3 1177, 1904 Beobachtungen uber Schussverletzungen der Bauchhohle in Friedenszeit, Arbeiten der propädeutischen chirurgischen Klinik von W A Opel, 1910, vol 1, abstr., Centralbl f Chir 38 514, 1911	11	1	36.3	From the Surgical Clinics of Prof J Ederoff and W A Opel, Military Medical Academy. Of 11 patients, 7 recovered and 4 died, the injury operation interval was 1 hr for 9, 3 hrs for 1 and 7 hrs for another, the last 2 patients both dying in 1 who recovered, the bullet entered the stomach and later passed by way of the bowel.
Frolloff V I Diagnosis and Treatment of Penetrating Wounds of the Abdominal Cavity in Time of Peace, Voenno med J (med spec pt) 215 37, 249 and 459 1906	13	4	46.1	From the Munipal Hospital, Batum, Russia. Reports are given on 11 male and 2 female patients. The youngest was 13, the oldest 50, 7 patients recovered and 6 died of those recovering, 5 had only wounds of the intestines 1 had only a wound of the liver and 1 had no visceral injury of those dying, 5 had wounds of the stomach only and 1 had wounds of the colon only. The injury operation interval was stated to be from "immediately" to 24 hrs after injury. In one patient an overlooked wound of the gallbladder was found post mortem.
Imbert, I I tuda du pronostic dans les laparotomies pour plaies pénétrantes de l'abdomen, Cong franç de Chir Proc verb 20 259, 1907	17	Some made	70.4	1 from Versailles, France. Seventeen patients had bullet wounds 13 died and 35 had laparotomies, but injuries due to stabbing and those due to shooting are for the most part discussed indistinctly.
von Hofmann, A Ueber Friedensschussverletzungen Beitr 2 klin Chir 53 778 1907	11	0	55.5	From Beck's clinic in Karlsruhe, Germany from 1897 to 1907. Six patients died, 1 dying of tetanus 10 days after the injury.

debated Reclus, who headed the noninterventionists finally in 1905<sup>16</sup> announced his conversion to speedy laparotomy Nancrede asked the members present at the meeting of the American Surgical Association in 1887 to express an opinion on the question "Should laparotomy be done for penetrating gunshot wounds of the abdomen involving the viscera?"<sup>17</sup> At the meeting of the New York State Medical Association in 1886 a symposium on shot wounds of the intestines was held, in which a number of conspicuous American surgeons took part<sup>18</sup> This second epoch was also characterized by the publication of tables listing reports of laparotomies for abdominal bullet wounds almost as fast as they were announced Table 1 shows the essential features of a number of such collections

*Comment on Table 1*—Morton claimed that the list of laparotomies published with his first article<sup>13</sup> was the first collective summary made and that MacCormac<sup>19</sup> included it as an appendix to his oration In Barnard's thesis, which appeared the same year, there are two tables All the tables put forth subsequently by different authors have as their nucleus the reports of laparotomies listed by MacCormac, supplemented by others to complete the number made to date In a few reference to the more obvious operations for debridement are omitted

The operation performed by Pirogoff<sup>20</sup> found a place in several of these early compilations It was not included by Morton in the table accompanying his first article By Barnard it was classified as a debridement But the patient was lost sight of a few days after the operation, and whether he died or recovered was not learned Consequently, many who were interested in reporting the progress of events in tables which included Pirogoff's operation as a laparotomy were required to calculate the mortality rate on one less than the actual number of cases listed in their tables A portion of the title of Barker's<sup>21</sup> article reads, "Continuation from Sir William MacCormac's List", that list referred to

16 In discussing a report by SIVARIAUD (Double plaie penetrante de la grosse tuberosite de l'estomac Plaie du foie par balle de revolver Intervention Guérison Bull et mem Soc de chirurgiens de Paris 31 845, 1905) and referring to the inferior equipment of hospitals in France he said "Mais maintenant il n'en est plus de même et depuis quinze ans je suis devenu interventionniste" (but now it is different and in the last fifteen years I have become an interventionist)

17 Tr Am S A 5 155 1887, Ann Surg 5 455, 1887, J A M A 8 607 (Mar 28) 1887

18 Tr New York State M A 3 93, 1887 M News 49 601, 1886

19 MacCormac William The Annual Oration on Abdominal Section for the Treatment of Intra-Peritoneal Injury, Brit M J 1 975 and 1031, 1887

20 Pirogoff, N Grundsätze der allgemeinen Kriegschirurgie Leipzig, F C W Vogel 1864 p 578

21 Barker, A E J Notes on Two Cases of Laparotomy for Penetrating Gun-shot Wound of the Abdomen Recovery in One, Brit M J 1 571, 1880



TABLE 2—Reports by Single Surgeons and from Particular Hospitals—Continued

References	Number of Patients	Deaths	Mortality (Percent)	Comments
Harris, G. L. Gunshot Wounds of the Abdominal Cavity, with Report of Cases, Surg., Gynec. & Obst. 1916	18	0	33.8	From the Mercy Hospital, Pittsburgh. Seven of the 18 patients died. The average injury operation interval was about 9 hrs. for those who died. It was about 6 hrs. for those who recovered. It was about 14 hrs.
Goltman 61	12	2	73.8	From the General Hospital, Memphis, Tenn. Fourteen surgeons performed operations. Data are given on 12 patients who underwent operations. 31 died.
Smutal, W. Ueber Stieh und Schussverletzungen des Bauches, Wien med. Wochenschr. 70: 633, 1238, 1306, 1342, 1362, 1347 and 1362, 1920. Finsterer H. Zur Diagnose und Therapie der Leberverletzungen, Beitr. z. klin. Chir. 119: 398, 1920.	18	3	33.3	From Hocheng's clinic in Vienna, from 1900 to 1920. Smittal reports the occurrence of wounds of only hollow viscera in 8, of only solid viscera in 2, and of wounds of both types in 2 patients. Twelve patients recovered; 1 died, all the patients were males, the average age was 27½ yrs. Overlooked wounds of the right lung, liver and diaphragm were found in 1 body. For the patients who recovered, the average injury operation interval was 5½ hrs., for those who died it was 12 hrs. Finsterer adds a report of 1 case in which a wound of the liver and one of the colon caused death.
Kleinschmidt, O. Ueber Bauchschuss und Schloek, Arch. f. klin. Chir. 117: 569, 1921.	22	8	63.6	From political riots in Leipzig, Germany. Fourteen of the 22 patients who had laparotomies died. 3 others entered moribund and died without operations. The 22 laparotomies were performed within 3 hrs. after injury. 9 patients were between 9 and 13 yrs. old, 10 deaths were attributed to bleeding wounds of one ureter in 1 body, of the colon in a second, of the small bowel in a third, overlooked at the time of operation, were found post mortem.
Irmer, C. Gunshot Wounds of the Abdomen. Report of Cases, Kentucky M. J. 19: 501, 1921. Gunshot Wound of Abdomen Followed by Subphrenic Abscesses. Continued Report, Kentucky M. J. 20: 104, 1922.	13	One mentioned	69.2	From the City Hospital, Louisville, Ky. Eight surgeons performed operations. 9 of the 13 patients died. The average injury operation interval was about 1½ hrs. Detailed protocols are given for only 7 patients. One reported on in 1921 as having recovered died (see Farmer's second article) of an overlooked perforation of the back wall of the stomach and a subphrenic abscess.
Pratt, D. Heridas del abdomen por arma de fuego, An. de Fac. d. med., Montevideo 6: 455 (July) 1921.	15	1	10.0	From Montevideo, Uruguay. Five patients died of solely abdominal and 1 of thoraco abdominal wounds. In the single necropsy mentioned, an overlooked wound of the colon was found, a woman recovered after 6 holes in the bowel and 1 in the mesentery were repaired, a man who recovered had 16 perforations in the small bowel and 1 in the mesentery.
Valc 22	80	0	41.0	From the Receiving Hospital, Detroit, from 1920 to 1923. There were 67 male and 13 female patients. 30 Negroes and 50 white patients. 35 died. 9 deaths occurred in the operating room. There were multivisceral wounds in 50, a wound of a single viscus in 26 and no viscera injured in 4 cases. From the Gouverneur Hospital, New York, from 1911 to 1922. Operations were performed by different surgeons. 16 were on men, 2 on women and 1 on a patient whose sex was not stated. Eight patients recovered. 1 of these had 8 perforations of the bowel and 6 melæces (15.24 cm.) of the bowel was resected (Murphy button).
Condit, W. L. Perforated Gunshot and Stab Wounds of the Abdomen, Ann. Surg. 80: 51, 1924.	19	1	45.0	

wounds of the intestine are "far from being rare in civil practice, especially in America where everyone carries a revolver and often uses it on small provocation. We have been unable to find many references to bullet wounds of the abdomen in the Italian literature. Apparently, stabbing was and has continued to be the more favored practice in Italy. The introduction of the use of laparotomy for bullet wounds was definitely an American contribution to surgery, notwithstanding the fact that the first recovery from such an operation was reported by Kocher<sup>24</sup>

This practice was introduced more particularly by surgeons in the southern states where shooting was especially frequent among both white persons and Negroes. Brown<sup>25</sup> said in 1898 "I have no doubt but that there have been several hundred gunshot wounds of the abdomen, probably a thousand, in the last ten or twelve years in Birmingham, Ala., and the surrounding districts." The Charity Hospital in New Orleans has been referred to as a laboratory for research on bullet wounds. During a single decade from 1900 to 1910, more penetrating wounds of the abdomen stab wounds and bullet wounds were observed there than were sustained by the American forces in the entire Spanish-American War.<sup>26</sup> Loria<sup>27</sup> said that 1 299 patients with bullet wounds of the abdomen were admitted in the years from 1900 to 1931 inclusive. In 1925 a committee on gunshot wounds of the abdomen was appointed at the aforementioned hospital,<sup>28</sup> Loria was secretary and Matas, chairman. The habit of promptly performing laparotomy as a routine in cases of bullet wound of the abdomen spread so rapidly that frequently the operation was successfully carried out under extremely adverse conditions e. g. in cabins of Negroes in box cars, on plantations remote from conveniences usually regarded as essential and without skilled help, etc. An extensive dissertation could readily be written about this single phase of the development of abdominal surgery.

Conner<sup>29</sup> found that 174 of the 188 laparotomies regarding which he was able to obtain information were performed by fifty-five American

24 Kocher, T. Schusswunde des Magens mit rasch eintretenden peritonitischen und Collapserscheinungen. Laparotomie 3 Stunden nach der Verletzung, Magen-naht. Heilung. *Cor-Bibl. Schweiz. Aerzte* 13: 598, 1893.

25 Brown, G. S. in discussion on Grant H. H. The Practical Management of Bullet Wounds of the Abdominal Viscera, *Tr. South Surg. & Gynec. A.* 11: 50, 1898.

26 Van Scharck H. D. Penetrating Wounds of the Abdomen, *J. Florida M. A.* 14: 33, 1927.

27 Loria, F. L. The Influence of Hemorrhage in Abdominal Gunshot Injuries, *Ann. Surg.* 96: 169, 1932.

28 Loria, F. L. (a) Visceral Injuries in Gunshot Wounds of the Abdomen, *New Orleans M. & S. J.* 80: 283, 1927, (b) Prognostic Factors in Abdominal Gunshot Wounds, *ibid.* 83: 393, 1930.

29 Conner P. S. Laparotomy in Cases of Gunshot Wounds of the Abdomen, *Tr. Pan-Am M. Congr.* 1893, Washington, D. C., Government Printing Office, 1895, pt. 1 p. 691, abstr., *J. A. M. A.* 21: 431 (Sept. 16) 1893.

surgeons and that 123 deaths resulted. In the much smaller group in Moiton's first collection, 18 of the 22 operations were performed in this country. Following the successful operations by Kocher,<sup>24</sup> Bull<sup>30</sup> and Hamilton<sup>3</sup> the expediency of performing laparotomies for bullet wounds of the abdomen was quickly recognized, and the practice was adopted in America. The number of such operations soon became too large to be recorded in tables, and the publication of such tables gradually ceased. In the preface to their monograph Martin and Hare wrote "We have collected and placed before the reader what we believe to be the fullest statistics yet collected upon gunshot wounds of the abdomen." Their work was awarded the Fiske Fund Prize on July 12, 1890. They did not state when their manuscript was finished.

Many authors have commented on the unreliability of the mortality rates contained in the early literature on laparotomies for bullet wounds of the abdomen.<sup>31</sup> This is based, of course, on the disposition to report only the successful operations. In order to lessen this error, Conner<sup>29</sup> obtained his figures from answers to a questionnaire sent to prominent American surgeons. Replies came from seventy-three, of whom eighteen had never performed operations for bullet wounds of the abdomen. He asked that the whole number of laparotomies performed by each surgeon as well as the number in which recovery occurred be given.

Publication of the accomplishments of single surgeons or the experiences at particular hospitals marks the third period in the recital of conspicuous stages of the development of modern methods of treatment of bullet wounds of the abdomen. We are now in this epoch which is well along toward completion. The evolution of any special improvement in surgery is apparently marked by similar features: a time when the demand for a new operative treatment is a matter of common agreement but methods are still undevised, a period marked by announcements in "case reports" that the difficulties are overcome, collection and publication in tables of successful operations of the type under consideration, the third period, already defined, ending when mortality rates are fairly stable and reports published by single surgeons of their results with large numbers of the new operation no longer command the attention they formerly received. Table 2 deals with this third period.

DATA COMPARABLE WITH THOSE FROM THE COOK COUNTY HOSPITAL

*Comment on Table 2*—Table 2 is based on what data we have been able to find in the literature suitable for comparison with the products of our examination of the records of the work done at the Cook County

30 Bull, W. T. A Case of Gunshot Wound of the Intestines Treated Successfully by Laparotomy with Suture of the Intestines, *M. News* 46 171, 1885.

31 The comment of Imbert (*Étude du pronostic dans les laparotomies pour plaies pénétrantes de l'abdomen*, *Cong. franç. de chir.* 20 259, 1907) is particularly just and thoughtful.

McAfee, I. W. Penetrating Wounds of the Abdomen with Report of Cases. Tr South S. & Gynce A 11 22 1893	15	4	606	From the Grady Hospital, Atlanta Ga. from 1898 to 1908 The first 2 of the 4 articles are almost identical. Altogether McKee reported on laparotomies on 15 patients, the results were as follows 10 deaths and 5 recoveries. 6 Negroes, 4 white persons and 5 whose race was not stated. The injury operation interval was short, as a rule of the patients who recovered 1 had wounds of only the stomach, 3 of only the ileum, 1 of only the liver and 1 of only the urinary bladder and ileum, in 1 body an overlooked wound of the colon was found post mortem.
Oliver, J. O. Fifty Eight Cases of Gunshot Wounds of the Abdomen. Lancet Clinic 40 463, 1898. Caldwell, O. L. Penetrating Wounds of the Abdomen, with Report of Cases Including a Case of Traumatic Rupture of Congenital Cystic Kidney. Tr South S. & Gynce A 18 398, 1906	26	14	692	I from the Cincinnati General Hospital, Cincinnati. Oliver's report deals with laparotomies performed by himself and 4 other surgeons for penetrating bullet wounds of the abdomen in 22 patients. Caldwell deals with 1 patient's Comments are also made in each report on 1 case of a non penetrating bullet wound of the abdomen. Seventeen of the 26 patients died. Overlooked wounds were found in 8 of the 11 bodies examined after death. Caldwell reported 1 death and 3 recoveries.
Vaughan, G. T. Gunshot Wounds of the Abdomen. Ten Intestinal and Twelve Perforations of the Mesentery. Operation, Recovery. M. News 73 113, 1893. Gunshot Wounds of the Uterus. Two Cases of Uterovesical Anastomosis, Am J M Sc 129 449 1903. Gunshot Wounds of the Abdomen, a Review of Fourteen Cases with Remarks on the Mortality and Treatment, Am J M Sc 131 255, 1906. Further Remarks on the Treatment of Gunshot Wounds of the Abdomen, with Especial Reference to the Treatment of Wounds of the Urinary Bladder and the Danger of Abscess and Fistula Following Wounds of the Funerics, Am J M Sc 131 266, 1907	17	1	538	Report on surgical experiences in Washington D. C. from 1898 to 1907 17 patients 9 of whom died. 1 had multiple perforations of the ileum and a resection followed by death. Another who died had a bruised bowel and hemorrhage from a wound made by a blunt cartridge, a third recovered from a bullet perforation of 1 ureter. The remaining 11 had wounds of 2 or more viscera.
Shinoas, M. Gunshot Wound of the Abdomen, Tr South S. & Gynce A, 12 45 and 263, 1900	20	None mentioned	850	Report by Shinoas, professor of surgery at Charleston, S. C. There were 20 cases with 17 deaths. 1 patient with 15 holes of the small bowel 1 with 2 ft (60.96 cm) of the small bowel resected and 1 third with 2 holes in the stomach recovered. Many of the 20 patients were Negroes and were transported long distances. The average injury operation interval was about 20 hrs.
Nietert, H. L. Report of a Case of Gunshot Wound of Pregnant Uterus and Fetus. Cesarean Section, Recovery, M Rev 41 303, 1900. Penetrating Wounds of the Abdomen, Interstate M J 9 599, 1902	17	0	538	From the City Hospital, St. Louis. Data are given on 17 patients 7 of whom recovered and 10 died, 7 dying of hemorrhage and shock during or immediately after operation. A woman 7 months pregnant recovered from a wound of the uterus and cesarean section, the fetus had a wounded shoulder and died of prematurity. Necropsies are not mentioned.
Tantzseher, K. Zur Behandlung der perforierenden Bauchwunden, Samml klin Vorträge, n. f., Leipzig, no 319 (Chir no 91, p 247) 1901. Brehm, O. Resultate bei den penetrierenden Bauchverletzungen des Fricdens, Arch f klin Chir 73 234, 1904. Michelsson, F. Zur Diagnose und Therapie der Schussverletzungen der Milz, Deutsche Zeitschr f Chir 124 323, 1913	20	1	320	From A. von Bergmann's clinic at Riga, Latvia. Tantzseher had 8 cases with 1 death. Brehm had 7 with 2 deaths. Michelsson had 5 with 1 death. One of Brehm's patients who recovered had wounds of the liver, stomach, spleen and splenic artery and underwent a splenectomy. The causes of death were as follows: wounds of the colon 4, wounded spleen and peritonitis, 1, wounded liver, 1, and peritonitis without visceral injury, 1.
Summers, J. E. Personal Experiences with Contused Gunshot and Stab Wounds, West M Rec 7. 107, 1902	10	0	700	From private practice in Omaha. Reports are given of 7 deaths, 5 from hemorrhage and 2 from peritonitis. Of the patients who recovered, 1 had no viscera injured, 1 had a wounded kidney, and 1 had wounds of 1 lung, the liver and spleen.

from 1897 to 1907 In the inaugural dissertation by Angerer<sup>33</sup> there are accounts of laparotomies performed in that clinic for bullet wounds on 4 patients in 1897 and on 1 in 1901 These cases are probably also reviewed in the article by Gebele and in that by Bestelmeyer or in both A similar statement applies to two cases in which treatment given at that clinic in 1901 and 1904 is described by Riester<sup>34</sup> Observations in the St. Louis City Hospital, recorded by Marks, Nietert and Brown, each of whom gave data for a different period, presumably pertain to different patients, but Steckbauer, whose article appeared much later, failed to state when he performed laparotomies for bullet wounds of the abdomen on 26 patients in the aforementioned hospital Some of the 43 cases of laparotomy for such wounds mentioned by Besley and James are probably included in our series They covered all varieties of penetrating wounds of the abdomen, and those due to bullets received less consideration than those caused in other ways The report of one of the patients cared for by Straus<sup>35</sup> is included in our series Richter<sup>36</sup> mentioned the cases of 8 children with bullet wounds of the abdomen cared for in the Cook County Hospital Two of these 8 cases are included in our series, in both recovery occurred A third case in our series is included in the report by Levin,<sup>37</sup> whose article is based on Richter's material as well as on additional observations made at both the Mount Sinai Hospital and the Cook County Hospital in Chicago The third child also recovered All 3 children had laparotomies Levin failed to state when the observations he reported were made They probably concern a period subsequent to that covered by our series The reports from von Bergmann's clinic by Tantzsch, Brehm and Michelsson deal with patients cared for at that clinic from 1904 to 1908 The fourth report is by Jankowski<sup>38</sup> He, unfortunately, failed to indicate the mortality rate for bullet wounds separately from that due to other causes Consequently his information cannot be included with that contained in the reports by Tantzsch, Brehm and Michelsson Michelsson's study was limited to bullet wounds of the spleen as observed in the clinic at Riga, Latvia, during the period from 1890 to 1912 He found that 10 patients had been treated for such injuries, but only 6 of the 10 had undergone laparotomies Brehm had previously described the injuries in 1 of those

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33 Angerer, T Ueber Stich- und Schussverletzungen des Magens, Munich, Kastner & Callny, 1903

34 Riester, H Milzextirpation nach Schussverletzung, Wurzburg, J Meiner, 1912

35 Straus, D C Recent Gunshot Wounds of the Kidney with Report of Four Cases, *S Clin North America* 2 635, 1922

36 Richter, H M, in Abt, I A Pediatrics, Philadelphia, W B Saunders Company, 1924, vol 3, p 485

37 Levin, I M Abdominal Injuries in Children, *Ann Surg* 87 718, 1928

38 Jankowski, J J Ueber penetrierende Stich- und Schusswunden des Bauches, Inaug Dissert, Riga, 1909 (Russisch), *Centralbl f Chir* 37 581, 1910

Bestelmeyer R Chir 55 637, 1907	Ueber Schussverletzungen, Beitr z klin	17	9	30	From the Angerer Clinic of Munich, Germany from 1897 to 1907 Of 9 patients who died, 3 entered moribund In 1 body a wound of the duo denum, and in another a wound of the left lung, was undiscovered at the operation
Riebel, F C 4 202 1907	Abdominal Gunshots, Surg, Gynce & Obst	26	0	34 6	From Chicago At the Provident Hospital 11 patients underwent laparotomies at the People's Hospital, 15 Dr W E Schroeder operated on 18, Dr Riebel, on 9, for 1 the surgeon is not named There were 25 males and 1 female 15 Negroes and 11 white patients Nine patients died Of 9 with thoraco abdominal wounds, 4 recovered, 3 of 4 patients with resections of the bowel recovered, 1 recovered after splenectomy and nephrectomy
Després, J	Vingt ans de plaies pénétrantes par balles de revolver, crâne, thorax, abdomen, fœtus, Cong franç de chir Procès verb, mém et disc 21 932, 1908	20	7	40 0	Report on surgical work by Després at Toulon, France, from 1900 to 1908 Eight patients died 4 of wounds limited to the stomach 1 of wounds limited to the omentum, 1 of wounds limited to the liver and 1 of injuries limited to the right kidney Recoveries occurred, no details of necropsies are given
Hagenborn J A	Ueber Bauchschüsse im Frieden und ihre Behandlung, Deutsche Zeitschr f Chir 92 1, 1908, Ueber Schussverletzungen im Frieden, Ibd 128 43, 1914	14	0	78 5	From the Municipal Hospital, Kyono, Russia Several surgeons performed operations 11 of the 14 patients died, 1 of wounds made by a toy cannon 1 recovered from wounds made by two bullets fired into the abdomen
Graham C	Gunshot Wounds of the Abdomen A Report of Nine Cases Seven Penetrating Wounds of the Viscera and Two Non Penetrating, Surg Gynce & Obst S 374, 1909, Gunshot Wounds of the Intestines, Kentucky, M J 11 209, 1912 1913	14	2 mentioned	35 7	From Graham's private practice in Henderson, Ky Twelve of the 14 patients were shot in front 2 were shot from behind in 2 of the 5 who died no abdominal viscera was injured, 1 had wounds of only the small bowel 1 had wounds of both large and small bowel (39 perforations in the latter), 1 had wounds of the stomach, colon and small bowel There were 11 male and 3 female patients
Okinschewitsch, A J	Penetrierende Stieh und Schusswunden des Bauches nach den Erfahrungen des Krankenhauses in Balakhany Sabuntshi von 1903 bis Mitte 1908, Baku, 1909 abstr Centralbl f Chir 37 583, 1910	21	0	66 6	From the hospital in Balakhany Sabuntshi, U S S R, maintained by industries for the preparation of naphtha employing Russians, Persians Armenians, etc Of the 7 patients who recovered, 3 had no visceral injuries, 3 had injuries of the stomach, and 1 had an injury of the colon, of those who died, 10 had wounds of the small bowel only, 2 of the colon only, 1 of the liver only and 1 of the colon and small bowel The injury operation intervals and necropsies are not mentioned From the Macon Hospital, Macon, Ga from 1909 to 1910 Six different surgeons performed operations 8 patients died 2 dying on the table 7 recovered There were 14 males and 1 female, 13 Negroes and 2 white patients Two patients who recovered had no abdominal viscera wounded the average injury operation interval for the patients who recovered was 3 75 hrs, for those who died, 7 25 hrs
Braneh, J R B	Penetrating Wounds of the Abdomen, Ann Surg 54 164, 1911	15	None mentioned	50 3	From the Cook County Hospital, Chicago A number of surgeons per formed operations, 22 of the 43 patients died
Besley, J A, and James, W A	The Time Element in the Operative Treatment of Abdominal Injuries, with a Consideration of 172 Cases Taken from the Records of Cook County Hospital, Illinois M J 25 87, 1914	43	No details	51 0	
Crawford, L B	Gunshot Wounds of the Abdomen, Statistics from Charity Hospital, 1906 1913, and Reports of Two Cases Operated On, New Orleans M & S J 67 1, 1914	52	0	61 0	From the Charity Hospital, New Orleans, from 1906 to 1913 A number of surgeons performed operations, 22 of the 52 patients who had laparotomies died
Camaggiato 20		117	0	61 5	From the Pellegrini Hospital in Naples, Italy, from 1901 to 1914 Two hundred and sixty eight patients were treated for bullet and stab wounds of the abdomen 19 had injuries from blunt force Consideration of the different types of injury by Camaggiato is impractical and essential One hundred and seventy seven of the patients wounded by bullets had laparotomies, 70 recovered No information about necropsy or the injury operation interval is given

wound with protruding gangrenous loops of small bowel was found at the postmortem examination, the interval between the injury and the operation was seventeen hours, forty-three small perforations in the small bowel were repaired, death occurred two weeks after entrance to the hospital and resulted from peritonitis and sepsis with multiple small pulmonary embolic abscesses

The mortality from shotgun wounds is high. Many of the victims are shot at close range. Bunch,<sup>41</sup> of Columbia, S. C., had 7 patients

TABLE 3—*The Cook County Hospital Series*

Sex	Number	Died	Average Age (Years)	Necropsies	Mortality (Percent age)	Recovered	Average Age (Years)
Male	303	199	32.5	184	65.5	104	29.5
Female	40	23	35.1	21	57.5	17	25.3
Total	343	222	33.8	205	64.7	121	27.4

TABLE 4—*Data on Patients Who Had Laparotomies*

Sex	Number	Died	Average Age (Years)	Necropsies	Mortality (Percent age)	Recovered	Average Age (Years)
Male	268	169	31.9	155	62.6	99	25.9
Female	33	16	34.3	14	48.5	17	29.3
Total	301	185	33.3	169	61.4	116	27.6

TABLE 5—*Data on Patients Who Had no Laparotomies*

Sex	Number	Died	Average Age (Years)	Necropsies*	Mortality (Percent age)	Recovered	Average Age (Years)
Male	35	30	32.6	29	85.7	5	27.7
Female	7	7	34.7	7	100.0	0	—
Total	42	37	33.7	36	88.0	5	27.7

\* The one body not examined after death was that of the only patient among the 343 with no operation and no necropsy. 16 others had operations but no necropsies. The 17 were removed from the morgue by "orders from the Central Office."

with such wounds in fifteen years, 2 recovered. In 1 of these 2 the liver was the only viscus wounded. In the other, every coil of bowel had many small perforations, and about twenty shot were free in the abdomen. Willis<sup>42</sup> referred to 14 patients with shotgun wounds whom he saw at Rocky Mount, N. C., 4 died and 3 recovered without operations, of the 7 who underwent laparotomies, 4 recovered. He also mentioned that when repairing the wounds made by a bullet in another patient he

41 Bunch, G. H. Shotgun Wounds of the Abdomen, *Tr. South S. A.* 41: 38, 1928.

42 Willis, B. C. Penetrating Wounds of the Abdomen. Reporting Sixty-Three Cases Received from Pistol, Rifle and Shotgun Missiles, *Ann. Surg.* 96: 161, 1932.

Hauser, C D Traumatic Perforations of Abdominal Viscera, Ohio State M J 21 162, 1925	17	0	23 5	Report on surgical work by Hauser and his colleagues in Youngstown, Ohio Data are given on 17 patients, 1 died and 13 recovered 2 pregnant women had wounded uteri in 1 the fetus was killed by a bullet, the other under went a cesarean section the delivered child and both women recovered 7 patients who recovered had multiple perforations of the bowel as follows 11, 8, 8, 7, 6, 6 and 1 2 died and 1 recovered after splenectomies Report on surgical work by Davis in Nashville, Tenn Four of the 13 deaths were from thoracic abdominal wounds
Davis M B Gun Shot and Stab Wounds of the Abdomen An Observation of Twenty Eight Cases and the Immediate Final Results J Tennessee M A 18 190, 1925 Steckbauer, J W Gun Shot Wounds of the Abdomen in Civil Life, Wisconsin M J 25 179, 1926	20	0	65 0	
	26	14	53 8	From the St Louis City Hospital, St Louis Steckbauer performed laparotomies on 26 patients 12 recovered and 14 died, 11 of peritonitis and 3 of shock There were 22 male and 4 female patients 15 were white persons and 11 were Negroes The injury operation interval and the dates of the operations are not stated in 2 bodies overlooked perforations were found after death, the location was not stated From the Grady Hospital Atlanta Ga Data are given on the work of various surgeons, 40 of the 63 patients died, 8 dying from 1 to 7 hours after admission
Blais, C Treatment of Gunshot Wounds of the Abdomen, J M A Georgia 16 166, 1927	66	0	69 6	From the Charity Hospital, New Orleans Forty seven patients died and 29 recovered the injury operation interval in most cases was 2 hours or less In reference 334 factors influencing the prognosis in this series are discussed
Loria 35	76	0	61 8	From the Charity Hospital, New Orleans Forty seven patients died and 29 recovered the injury operation interval in most cases was 2 hours or less In reference 334 factors influencing the prognosis in this series are discussed
Miller, M O Gunshot Wounds of the Abdomen, New Orleans M & S J 50 279, 1927	46	0	56 5	From the Charity Hospital, New Orleans, from July 1, 1925 to June 13, 1927 Twenty six patients died, 31 of the 46 patients were Negroes, 38 being male and 8, female
McKeithen A M Penetrating Wounds of the Abdomen a Study of Sixty Nine Cases, Kentucky, M J 27 77, 1929	56	0	44 6	From the City Hospital, Louisville, Ky Twenty five patients died
Billings and Walking 31	114	50	48 2	From the Pennsylvania Hospital, Philadelphia, from 1909 to 1930 Fifty five of the 114 patients died in 11 of the 50 necropsies, overlooked wounds were found, in 6 of the 11 bodies there were such overlooked wounds of 2 or more organs, and in the remaining 5 bodies wounds of a single organ were overlooked
Wills 42	58	0	25 8	Report on surgical work at Rocky Mount, N C About five sixths of the patients were Negroes, 15 died The wounds in 10 were made with the missiles from shotguns, 4 patients recovered
Oddone, G S Consideraciones sobre 38 casos de abdomen agudo traumático con lesión de vísceras huecas Resúmen operatorio, Bol y trab de la Soc de cir de Buenos Aires 17 267, 1933	16	0	31 0	Oddone worked in Cordoba, a province of Argentina, 5 patients died
Prey, D, and Foster, J M Gunshot Wounds of the Abdomen, Ann Surg 99 265, 1934	22	0	72 7	From the Denver General Hospital, Denver Fifteen of the 22 patients died for those who recovered, the average injury operation interval was 188 hrs for those who died it was 34 hrs
Oberhelman and LeCount	701	169	61 5	From the Cook County Hospital, Chicago, from 1911 to 1934 One hundred and eighty six patients died, 37 surgeons performed operations



tinctive features and that accounts of them should not be interwoven with those of bullet wounds

The oldest patient in our series was a woman aged 70, the youngest, a boy aged 5 years, both recovered. Undoubtedly many factors contributed to the fact that the average age of the 343 patients wounded by bullets was 31.5 years. The relative youthfulness is of great interest and rather startling, but there is no justification for an attempt to discuss its causes here. Its influence on the mortality rate, 64.7 per cent, is indubitable.

Except for routine examination of the entire spinal cord, of the joints of the extremities and of the marrow of long bones, the postmortem examinations were quite thorough. All the important structures of the neck, including the large blood vessels, were examined. The parathyroid glands were not examined as a routine.

Microscopic examinations were made of the important viscera, of places with obvious gross disease, of the brain, of the brain stem and of the upper end of the spinal cord. At the time of the necropsy the removed brain was placed bottom uppermost in the skull cap and a dilute solution of formaldehyde U.S.P. (1:10) was run in the basilar and two middle cerebral arteries, first in one artery and then in another, clips being placed on the two vessels not receiving the solution at the time. The embalming was continued until the brain was firm. The brain was then placed in a jar containing solution of formaldehyde U.S.P. (1:10) for a week or two, then it was sectioned and examined grossly, and after that pieces were taken for microscopic study.

With few exceptions such necropsies were made on the bodies of 205 of the 222 patients who died. Of the 17 unexamined bodies, 1 was that of a patient who had not been operated on, the remaining 16 patients had undergone laparotomies. Some of these 16 were persons for whose suicide there was overwhelming evidence, the conditions in a few others were fully disclosed by the surgeons who also recovered the bullets. But most of the 17 bodies were unexamined by "orders from the Central Office." In other words, political or other influences prevented the necropsies. The total number of necropsies mentioned in the contributions briefly summarized in table 2 is only 146, undoubtedly many more were actually performed.

The 205 necropsies in our series (tables 4 and 5) include 169 bodies of the 301 patients who had laparotomies and 36 of the 37 who died without such operations. As far as could be ascertained clinically, most of the 42 patients who had no operations died of shock and hemorrhage. For the 36 whose bodies were examined after death the following data are recorded: 21 were moribund on entrance, the condition of 12 was poor, that of 2 was fair, and that of 1 was good. In this last patient a man aged 45, the entrance wound was a little below the right nipple.

Hospital We have arbitrarily included in this table only such reports as are concerned with laparotomies for penetrating bullet wounds of the abdomen performed on at least 10 patients by one or more surgeons in the same hospital or by one surgeon at different places. Laparotomies for nonpenetrating bullet wounds of the abdomen are not included. Unless strictly intra-abdominal structures or viscera were also injured we have also aimed to exclude wounds of the kidneys, ureters and extra-peritoneal portions of the rectum and bladder. Laparotomies for wounds made by bullets passing through the abdomen and kidneys, ureters or large blood vessels are included even though intra-abdominal viscera escaped injury. The facts presented by many writers we have been unable to use because they have considered bullet wounds and stab wounds indiscriminatingly. In some articles the statistics set forth in the text differed from those in the tables. In order to maintain uniformity, we have been compelled to make new calculations for mortality rates because the writers included the deaths of patients who died without operations with those of patients who died after laparotomies. Our study is definitely one of mortality rates *after* laparotomies. When an author reported additional experiences with bullet wounds of the abdomen in one or more subsequent articles, as did Hagentorn, for example, these reports are given a single place in the table.

The observations of D Barrow and D W Barrow father and son, of Lexington, Ky, are considered together, notwithstanding the lapse of time between them and the presumably improved surgical methods. The remarks apply to R Winslow and W Winslow of Baltimore. The bullet wounds of the abdomen sustained during street rioting in Leipzig and reported by Kleinschmidt are included in the table. They may be regarded as borderline injuries midway between wounds sustained in peace time and those sustained in war, but they were not from shrapnel or other missiles the use of which is peculiar to war. In many respects the wounds sustained in street fights, especially those from rifles, are like those sustained in war<sup>32</sup>. Street fights also occurred in Chicago during the race riots of July and August 1919, but only 1 victim of these riots with a bullet wound of the abdomen was received at the Cook County Hospital. This was a white man who died without an operation.

It is quite possible that overlapping occurs in the reports from some hospitals, different authors including accounts of the same patients. For example, Gebele's account is based on bullet wounds of the abdomen cared for in Angerer's clinic in Munich from 1897 to 1902 and that of Bestelmeyer deals with reports from the same clinic for the years

<sup>32</sup> Meixner, Karl. Schussverletzungen durch Handfeuerwaffen, Arch f Kriminol **75** 91, 1923. De, J C. A Medicolegal Study of the Calcutta Riots of 1926, Indian M Gaz **62** 479 (Sept) 1927. Meixner, K, and Werkgartner, A. Schussverletzungen im Strassenkampf, Beitr z gerichtl Med **7** 32 1928.

*Wounds of Single and Multiple and of Hollow and Solid Viscera, Wounds with One or More Bullets (Tables 6, 7, 8 and 9) —Patients with simple bullet penetration of the abdomen without visceral injury gener-*

TABLE 7—*Mortality Rate for Patients With a Single Wound and for Patients with More than One Wound of a Single Viscus*

Viscus	Single Wound				Multiple Wounds				Total		Comment
	Num ber	Re cov eries	Deaths	Mor tality (Per cent age)	Num ber	Re cov eries	Deaths	Mor tality (Per cent age)	Num ber	tality (Per cent age)	
Stomach	5	5	0	0 0	10	8	2	20 0	15	13 3	
Small Intestine	4	1	3	85 0	37	20	17	45 9	41	48 7	
Colon	5	2	3	60 0	12	7	5	41 6	17	47 0	
Liver	24	21	3	12 5	4	3	1	25 0	28	17 2	
Urinary bladder	1	1	0	0 0	2	0	2	100 0	3	66 6	
Kidney	3	3	0	0 0	0	0	0	0 0	3	0 0	
Blood vessels	1	0	1	100 0	0	0	0	0 0	1	100 0	Mesenteric artery
Total	43	37	10	23 2	65	38	27	41 5	108	34 2	

TABLE 8—*Mortality Rate After Laparotomies for (a) Wounds of Hollow Viscera, (b) Wounds of Solid Viscera, (c) Wounds of Both Hollow and Solid Viscera and (d) Simple Penetrating Wounds Without Visceral Injury*

Organs	Number	Recoveries	Deaths	Mortality (Percentage)
Hollow viscera	170	67	103	60 5
Solid viscera	36	27	9	25 0
Hollow and solid	84	18	71	84 5
Penetration of peritoneum only	11	9	2	18 1
Total	301	116	185	61 4

TABLE 9—*Mortality Rates After Laparotomies for (a) Wounds with a Single Bullet and (b) Wounds with More than One Bullet\**

	Total	Recoveries	Deaths	Mortality (Percentage)
Patients with abdominal wounds from only one bullet	262	111	151	57 6
Patients with abdominal wounds from more than one bullet	14	2	12	85 7
Patients with abdominal wounds from one bullet and thoracic wounds from a second bullet	3	0	3	100 0
Patients with abdominal wounds from one bullet and wounds of the extremities from other bullets	22	3	19	96 9
Total	301	116	185	61 4

\* One of 7 patients wounded in the upper part of the abdomen with more than 1 bullet recovered, 1 of 3 wounded in the lower part with more than 1 bullet recovered, 4 with bullets in both parts died. Only 1 of the 13 with wounds of the abdomen and upper extremities recovered, 2 of the 6 with wounds of the abdomen and lower extremities recovered, 3 with bullet wounds of the abdomen and both upper and lower extremities died. There were exit wounds in 32 of the 116 who recovered and in 62 of the 185 who died.

ally recover, except when infections develop in the path of the bullet, only 2 of the 11 patients (table 8) with such wounds died, both of peritonitis. Those with wounds of a single viscus (table 6) also usually

6 patients, and Jankowski had described those in 3. The other 2 cases were first mentioned in Michelson's article.

The common use in New Orleans of pistols and revolvers as weapons has led to more contributions from the Charity Hospital in that city than from any other single institution. Five authors, Miles, Parker, Crawford, Loria and Miller, who worked in New Orleans, are mentioned in table 2. Duplication by these authors, however, is probably only in the reviews of Loria and Miller, as they cover the same period from 1925 to 1928. Fenner's<sup>39</sup> summary, however, includes stab and bullet wounds of the abdomen treated at the Charity Hospital during the period from 1892 to 1901. Presumably his contribution embraces observations previously set forth by Miles in 1893 and by Parker in 1896. It is quite likely that further search would disclose reports from single clinics or hospitals<sup>40</sup> by several writers so that other groups of 10 or more cases could be added to table 2.

The total number of patients with bullet wounds of the abdomen with laparotomy collected from the literature in table 2 is 1,494, 789 of the patients died—a mortality rate of 52.8 per cent. The contributions in this table are arranged chronologically. Those published during the years covered by our series deal with 535 patients, of whom 300 died—a mortality rate of 56 per cent—as compared to 301 patients with 185 deaths—a mortality rate of 61.4 per cent—in our series. Concerning our own series we present the following comments as well as tables 3 to 18. In some of the tables there is overlapping, and this is explained in the footnotes to some of them for example, in the footnote to table 6.

#### COOK COUNTY HOSPITAL SERIES

*General Considerations (Tables 3, 4 and 5)*—The wounds were such as are usually produced by homicidal, suicidal and accidental shootings occurring in large cities. None of the 343 patients was wounded with the kind of machine-guns now used by gangsters. Strictly speaking, wounds due to the small lead pellets used in shotguns to shoot ducks and other wild game ought not to be included with bullet wounds of the abdomen. But following a practice set by other writers we have included the single shooting of this character with the other 342 occurring in the period covered by the series. The case was that of a man aged 23, who was shot in a fight in a saloon. A huge gaping laparotomy

<sup>39</sup> Fenner, E. D. Report of Six Cases of Penetrating Wounds of the Abdomen Submitted to Abdominal Section with a Statistical Table of One Hundred and Fifty-Two Cases Thus Operated on at the Charity Hospital in New Orleans, La, Ann Surg **35** 15, 1902.

<sup>40</sup> Such a search yielded the information regarding the 12 patients treated in von Bramann's clinic in Halle, Germany, reported by different authors over seventeen years. (See the second item in table 2.)

had wounds of two or more viscera. Of these, only 35 recovered, and 147 died, this reveals an astounding mortality rate of 80.7 per cent, as compared to that of 34.2 per cent for those with injuries to a single viscus. Of 23 who had wounds of viscera and large blood vessels, 21 died—a mortality rate of 91.3 per cent. The mortality rate was likewise high when the kidneys, pancreas and spleen were wounded together with other organs.

**Wounds of the Kidneys** Of the 343 patients in our series, 43 had bullet wounds of the right or left kidney, in no patient were there wounds of both kidneys. In 29 patients the left and in 14 the right kidney was injured. Operations were performed on 34 of the 43 patients, 10 of the 34 recovered and 24 died—a mortality rate of 70.6 per cent. Billings and Walkling<sup>51</sup> in their series of 114 patients with bullet wounds of the abdomen treated by laparotomy had 10 with wounds of the kidney, 3 recovered and 7 died—a mortality rate of 70 per cent. Of the 24 patients in our series who died after laparotomy, 19 were shot in front and 5 were shot from behind, 15 died of hemorrhage and shock, 8 of peritonitis and 1 of separation of the laparotomy wound. Of the 10 who recovered, 6 were shot in front and 4 from behind. In 3 patients in whom the kidney alone was injured, the bullet traversed the abdomen. These 3 recovered. In 31 patients other viscera also were injured, the stomach was injured in 16 patients, the colon in 12, the liver in 10, the small bowel in 9, the pancreas in 3, the spleen in 2, and each lung and each adrenal gland in 1 patient, respectively.

Wounds of the kidney overlooked by the surgeon at the time of operation were found subsequently at autopsy in 18 of the 24 patients who underwent operations. In 4 of 7 patients who died and had undergone operations, Billings and Walkling<sup>51</sup> found such overlooked wounds. In the 18 patients of our series, wounds of the left kidney were overlooked in 11 and wounds of the right kidney, in 7. Hemorrhage and shock accounted for death in 13 patients, generalized peritonitis caused death in 4, and separations of the laparotomy wound caused it in 1. The 9 patients who were not operated on died, and all had wounds of other viscera besides wounds of the kidneys, 4 were shot from behind and lived for an average period of two and a half days, 5 who were shot in front lived for an average period of three hours.

**Wounds of the Pancreas** There are relatively few reports of cases dealing with peace time bullet wounds of the pancreas whether alone or associated with wounds of other viscera. At the time he made his report Becker<sup>53</sup> stated that his was the only case in the literature in which the pancreas was the sole viscus injured. Berendes<sup>54</sup> attended a patient

<sup>53</sup> Becker, A. *Isolierte Schussverletzung des Pancreas, durch Operation geheilt*, Beitr. z. klin. Chir. **44** 748, 1904.

<sup>54</sup> Berendes. *Pankreasschuss*, Centralbl. f. Chir. **38** 163, 1911.

found two bird shot in the liver and 1 in the gallbladder from a former shooting

One of 4 patients with shotgun wounds reported on by Ewstifejewa<sup>43</sup> recovered. This patient had a generalized peritonitis when the laparotomy was performed three days after the shooting. Only a few perforations of the small bowel were found. The missiles in the cartridge were nails, and they had entered the lower part of the abdomen.

Most of the reports of shotgun wounds deal with single patients who recovered. Pels-Leusden's<sup>44</sup> patient had a thoraco-abdominal wound, the omentum, transverse colon and food-distended stomach entered the left pleural cavity through a huge rent in the diaphragm, and the spleen was in fragments. Another recovery reported by Waters<sup>45</sup> was that of a boy, aged 15, who was shot at close range. The stomach projected like a football carried under the left arm. In this patient also the spleen was extremely torn.

The patients of Foisy<sup>46</sup> and Cochez and Pieri<sup>47</sup> were both shot in the back, recovery was protracted, and two or more operations were performed.

A man who attempted suicide by shooting himself in the left hypochondriac region with a shotgun and was treated by Estes<sup>48</sup> left the hospital after fifty-six days, having undergone removal of the left kidney. Cannada,<sup>49</sup> on the other hand, in recording the data on bullet wounds in 7 patients included the wounds made by small shot in a Negress, who died seven days after he had repaired thirty-eight perforations in the small bowel, colon, stomach and gallbladder.

The purpose of this discussion of shotgun wounds is to emphasize the statement that they deserve a separate place, that they possess dis-

43 Ewstifejewa. Verletzungen der Bauchhöhle. Zusammenstellung des Materials des Smolensker Gouvernements-Krankenhauses für 2½ Jahre, 32 Fälle, Russk. v. Arch. **12** 402, 1913.

44 Pels-Leusden. Milz und Zwerchfellverletzung, Verhandl. d. deutsch. Gesellsch. f. Chir. **33** 95, 1904.

45 Waters, C. H. Gunshot Injury of the Thorax with Extrusion of the Entire Stomach and Laceration of the Spleen, J. A. M. A. **73** 1577 (Nov. 15) 1919.

46 Foisy, E. Blessure de l'ampoule rectale et l'intestin grêle par coup de fusil de chasse. Laparotomie, suture de la perforation de l'intestin et exclusion du rectum. Occlusion intestinale le 38<sup>me</sup> jour par bride épiploïque. Section de la bride. Fermeture ultérieure de l'anus iliaque, Guérison. Bull. et mem. Soc. de chirurgiens de Paris, **39** 1410, 1913.

47 Cochez and Pieri (d'Alger), Plaie du duodenum par arme à feu, anus contra naturam consécutif, gastro-enterostomie, guérison, Bull. et mem. Soc. de chirurgiens de Paris **51** 503, 1925.

48 Estes. Case of Small Shot Wound of the Abdominal Cavity, Laceration of the Spleen, Mesocolon and Kidney, and Probably Laceration of the Stomach also, Recovery, Tr. Am. S. A. **17** 257, 1899.

49 Cannada, J. E. Wounds of the Liver, Lancet-Clinic **57** 449, 1906.

died within five hours or less. In the bodies of these 6 patients twenty-five wounds were found at autopsy, among others six wounds were in the liver, three each in the stomach, left kidney and aorta, and one each in the left lung, renal vein, splenic vein and inferior vena cava.

**Wounds of the Spleen.** As for bullet wounds of the spleen, we wish solely to direct attention to their infrequent occurrence and to the high mortality rate incident on such wounds. As regards the former, the small size of the spleen and its protected position are important factors. The high mortality rate is due to the vascularity of the organ and to the fact that other closely adjacent important viscera are wounded also. The collection by Schaefer<sup>58</sup> in 1902 included both peace time and war time wounds in 71 patients, 20 of whom had laparotomies, 13 died and 7 recovered—a mortality rate of 65 per cent. Only 1 patient had a wound solely of the spleen. With considerable duplication Gircolaw<sup>59</sup> collected reports on 69 patients with bullet wounds of the spleen, he found only 2 with wounds solely of the spleen, 39 died—a mortality rate of 56.5 per cent. In his long article, Guibe<sup>60</sup> analyzed 108 reports from the literature on bullet wounds of the spleen. Many of the cases are from military surgical practice. In practically all the patients other organs were wounded in addition to the spleen. Among the 112 patients with bullet wounds of the abdomen, Loria<sup>28a</sup> found either at operation or at necropsy only 3 who had wounds of the spleen. One in whom only the spleen was injured recovered, 2 with additional wounds of other viscera died. No wounds of the spleen were found in the 58 patients with bullet wounds of the abdomen who underwent laparotomy studied by Willis<sup>42</sup>.

In our series, only 19 patients had bullet wounds of the spleen, in these the wounds occurred in combination with wounds of other viscera, 14 had laparotomies, and 5 had no operations. Of the 14 operated on, 1 recovered—a mortality rate of 92.8 per cent. The 5 who were not operated on died. Of those who underwent laparotomy, 11 were moribund on entrance to the hospital, only 3 were in fair condition. The interval between the injury and the operation was four hours or less for 10 patients, and for 4 others it was eight hours, seventeen hours, twenty-three hours, and forty-eight hours, respectively.

In the first twenty-four hours after operation, 10 of the 13 patients who died succumbed to hemorrhage and shock, 2 died on the table, 1 died two days after operation and was not examined post mortem, 2 died

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58 Schaefer, F. Die offenen Milzwunden und die transpleurale Laparotomie, Beitr. z. klin. Chir. **36** 761, 1902.

59 Gircolaw, S. S. Zur Frage zu den Schusswunden der Milz, Vrach. gaz. nos. 46 and 47, 1909, abstr., Zentralbl. f. Chir. **7** 255, 1910.

60 Guibe, M. Les plaies de la rate par coup de feu, Clinique, Paris **7** 435, 1912, Rev. de gynéc. et de chir. abd. **18** 491 and 583, 1912.

and the bullet lodged subcutaneously at a similar distance below the left nipple. Death occurred on the thirteenth day, and wounds were found in the ribs and liver, there were also a subphrenic abscess pleuritis and pericarditis. Twenty-one of the 36 patients had one entrance wound, 11 had two such wounds, and 2 had three. Thirty-three of the 36 lived, on an average, for six hours after entrance into the hospital. Large blood vessels were found to be wounded in 17, in 7 of these the aorta was injured. The wounds in 12 patients were thoraco-abdominal, that is to say, both abdominal and thoracic organs were shot by the same bullet. In one patient a bullet passing through the scrotum made seven perforations in a loop of small bowel there in a hernial sac. The average number of organs injured in the 36 patients was three, in 1 patient a

TABLE 6—*Mortality Resulting from Bullet Wounds of the Abdomen Involving (a) Only One Viscus and (b) Two or More Viscera*\*.

Viscus	Wounds of Single Viscera, Wounds of Large Blood Vessels				Wounds of Two or More Viscera			
	Number	Re coveries	Deaths	Mortality (Percent age)	Number	Re coveries	Deaths	Mortality (Percent age)
Stomach	15	13	2	13.3	63	13	50	79.3
Small intestine	41	21	20	48.7	100	22	78	78.0
Colon	17	9	8	47.0	83	14	69	83.1
Liver	28	24	4	14.3	32	7	45	86.5
Urinary bladder	3	1	2	66.6	15	1	14	93.3
Kidney	3	3	0	0.0	31	7	24	77.4
Blood vessels	1	0	1	100.0	23	2	21	91.3
Spleen	0	0	0	0.0	14	1	13	92.8
Pancreas	0	0	0	0.0	13	4	9	78.0

\* Of the 301 patients with laparotomies, 37 of the 108 with wounds of a single viscus or of only large blood vessels died a mortality rate of 34.2%. Of the 182 with wounds of 2 or more viscera (again including large blood vessels as viscera), 147 died—a mortality rate of 80.7%. Of 11 patients with unwounded viscera, 2 died—bullets entered the abdomen in these 11. There is overlapping in the right hand part of the table. For example, the 63 patients with wounds of the stomach and other viscera are counted again with the patients in whom the other viscera were wounded.

huge hemoperitoneum was present, and a single abdominal organ was wounded. On the whole, subsequent developments and observations justified the decisions that laparotomies on the 42 patients in this group should not be made.

Only two other reports deal with large numbers of patients. One is by Camaggio,<sup>50</sup> who discussed the treatment given at the Pellegrini Hospital in Naples to 177 patients with bullet wounds of the abdomen, the other is an account by Billings and Walkling<sup>51</sup> of 114 cases in which laparotomies were performed at the Pennsylvania Hospital in Philadelphia (table 2).

50 Camaggio, G. Altre 50 laparotomie per lesioni violente dell'abdome, *Gior internaz d sc med Napoli* 37 8, 1915.

51 Billings, A. E., and Walkling, A. Penetrating Wounds of the Abdomen, *Ann Surg* 94 1018, 1931.



buck shot would be properly designated thoraco-abdominal or abdomino-thoracic when both parts of the trunk are wounded. The wounds confined to the thorax and made by one bullet and those made by a second shot fired into the abdomen are neither thoraco-abdominal nor abdomino-thoracic, they are bullet wounds of the thorax and abdomen. One essential of thoraco-abdominal or abdominothoracic wounds is that the diaphragm is wounded. This wound is sometimes so close to its attachment that the path of the bullet is mainly in the inner part of the wall of the trunk.

Of the 31 patients who were operated on (table 10) 19 had thoraco-abdominal and 12 abdominothoracic wounds. In the 12 patients who were not operated on the wounds were thoraco-abdominal. Of the 31 patients who were operated on 25 were males. The youngest patient in that group was a girl aged 17, the oldest, a man aged 68. The average age of the 31 patients was 33 years. Only 1 of 20 patients whose condition was poor on entrance recovered, of 6 who entered in a fair condition, 2 recovered, as did 4 of the 5 whose condition on entrance was good. Two of those who underwent laparotomies died on the table, 9 died during the first twelve hours, two died during the second twelve hours, and 4 died on the second day. Why one patient lived five and another thirteen days without undergoing laparotomy was not learned. The patient who lived four days had an operation for the removal of a bullet from the left femoral artery. This is referred to in another part of the article.

In view of the high mortality it is pertinent to recall that Moorhead<sup>61</sup> while still an intern at the Cook County Hospital repaired the wounds in a 45 year old man who in attempting suicide so shot himself that the bullet, passing in above the left sixth rib in the nipple line, went through the diaphragm at the upper part of the spleen, again through the diaphragm and through the lower edge of the left lung. It then broke the left tenth rib and lodged against it. The man recovered. The operation was performed on Nov. 28, 1891, soon after admission. The shooting took place seventeen hours before entrance. The surgeon, J. B. Murphy,<sup>62</sup> in his oration on "Surgery of the Lung" at the meeting of the American Medical Association in Denver in 1898 referred to the opportunity the operation afforded of observing the way respiration affected the lung when the thorax was opened.

A large part of the information about thoraco-abdominal wounds has come from experience gained during the World War<sup>63</sup>. At that time it

61 Moorhead, E. L. Gunshot Wound of the Thorax and Spleen, Chicago M Rec 2 549, 1892

62 Murphy, J. B. Surgery of the Lungs, J A M A 31 151 (July 23) 1898

63 Bowlby, Voncken, J., Duval, P., and Jacob, Depage. Plaies thoraco-abdominales, Arch de med et pharm mil 69 341, 1918

recover, this is especially true if the injured organ is solid. Of 108 patients with wounds of a single viscus (table 6), 37 died—a mortality rate of 34.2 per cent, of the 31 who had injuries of a solid organ 4 died—a mortality rate of 12.9 per cent, and for the 76 who had injuries of a hollow viscus the mortality rate was 42.1 per cent.

**Wounds of the Stomach** In the 2 fatal cases of wounds limited to the stomach the interval between the injury and the operation was less than two hours, one patient died two hours after operation of hemorrhage, the other died twenty-two hours after operation of infection with gas bacilli. In cases of bullet wounds involving only the liver the mortality rate was also low, only 4 of 28 patients so shot died, all of complications. The only patients in this group with exit wounds were the 7 who recovered.

**Wounds of the Intestine** There is a great deal of evidence that bullet wounds affecting solely the colon are much more serious than wounds elsewhere in the gastro-intestinal tract. This is not true in our series, but only 17 patients in our series had such wounds. The average number of perforations in the colon in the 8 patients who died was three, the highest number of such perforations in any one patient, nine. These wounds were made by a bullet which traversed the trunk from side to side. Vale<sup>52</sup> reported the occurrence of a similar path followed by a bullet in a patient in whom injury was confined to the mesentery. The average number of perforations in the colon in the patients in our series who recovered was two and five-tenths perforations per patient.

The largest group with wounds exclusively of a single abdominal organ consisted of 41 patients with injuries of the small bowel or of the small bowel and its mesentery. This is to be expected because of the relatively large space occupied by the small intestine. The mortality rate, 48.7 per cent, is quite high, and death was usually due to peritonitis. The average interval between the injury and the operation in the case of patients who died was four and six-tenths hours, for the remainder it was three hours. The number of perforations apparently fails to influence the outcome, for the average number of perforations per patient discharged was five and seven-tenths, for those who died the average number was five and three-tenths. The largest number of perforations in any single patient was fifteen, and six of these were found after death. Of patients who recovered, fourteen perforations was the highest number found in any one patient.

**Wounds of Two or More Viscera** The true gravity of bullet wounds of the abdomen is displayed when two or more viscera are injured (table 6) and when the wounds are made by two or more bullets (table 9). Of the 301 patients in our series who had laparotomies, 182

<sup>52</sup> Vale, C. F. *Civilian Wounds of the Abdomen*, J. Michigan M. Soc. 22: 183, 1923.

wounds were of the upper or lower part of the abdomen, the mortality rate, 57.1 per cent, was less for patients shot from behind. The number of persons shot from one side is so small that the mortality rate has no significance. Apparently, many persons die when bullets pass across the lower part of the trunk, and more die from injuries caused by bullets passing from front to back and wounding the lower part of the abdomen than from similar injuries of the upper part of the abdomen. In the latter case the bullet passes through more solid viscera. Of course, in cases in which there is an exit wound or recognized subcutaneous lodgment at the end of a path through the trunk, surgeons of experience make quite accurate surmises as to the organs injured. Martin and Hare<sup>10</sup> contended that bullets are deflected by soft tissues. It is also possible that some paths are irregular because the bullets tumble end over end or because their force is about spent. In the cases forming the basis of this report the weapons were usually revolvers or pistols, not rifles, and consequently less than one third of the patients in our series had exit wounds. Only 8 of the 50 patients in Goltman's series<sup>64</sup> had exit wounds.

Lodgment of the bullet just beneath the skin after it has traversed the trunk implies that the driving force was exhausted. The toughness of the corium may also be recalled, from it leather is made. Some other information pertinent to, but not included in, the table concerns exit wounds and their absence. In 178 patients there were no wounds of exit, the mortality rate for that group was 59.1 per cent. In 29 patients the bullets lodged subcutaneously, the body was practically traversed. If these cases are added to the 94 in which exit wounds were present, the sum is 123, or 40.8 per cent of the 301 cases in which laparotomies were performed, for this group the mortality was 64.2 per cent. It seems reasonable to conclude that the greater force required to send bullets on through the body, or even to subcutaneous lodgment opposite the wound of entrance, causes more damage than less forceful shots. Another noteworthy phase of these matters, of course, is the fact that bullets have been known to drop out of the clothing when the patient or dead body is undressed. Although the mortality rate from injuries caused by bullets which traverse the trunk is higher by about 5 per cent than that from the other wounds, even this small difference has definite value because of the large number of patients concerned. The paths of a few bullets were unusual.

One crossed the body from right to left, the entrance and exit wounds being symmetrical in the nipple lines just above the costal margins, and passed through both lobes of the liver. A second patient had a wound

<sup>64</sup> Goltman, M. One Year's Experience (1916) with Gunshot Wounds of the Abdomen at the Memphis General Hospital, Surg., Gynec. & Obst. 26:217, 1918.

with a bullet wound limited to the pancreas and located at the junction of the middle and distal thirds. In discussing this report, Nordman related his experiences in operating on a woman for an isolated wound of the pancreas two weeks after she had attempted suicide. Guleke<sup>55</sup> found reported in the literature only 31 cases of wounds of the pancreas, in 24 of these operation was performed, 11 patients recovered and 13 died.

In order to find any comprehensive investigation of bullet wounds confined to the pancreas one has to turn to the experiences related by military surgeons of the World War. The study of Wallace<sup>56</sup> on 965 patients who underwent laparotomy for wounds of the abdomen caused by missiles used in war disclosed that wounds of the pancreas alone were present in only 5 and that in 3 other viscera besides the pancreas were wounded. Fraser and Drummond<sup>57</sup> in studying material from a similar source found one patient with an injury to the pancreas among 300 with wounds of the abdomen made by missiles used in war.

In our series there were 19 patients with bullet wounds of the pancreas, and in all these wounds occurred in combination with injury of other organs, 15 died and 4 recovered—a mortality rate of 78 per cent. Of the 19 patients, 13 had laparotomies, 4 recovered and 9 died—a mortality rate of 69.2 per cent. The associated visceral injuries in these 13 patients were as follows: nine wounds of the stomach, six wounds of the liver, five wounds of the small bowel, three wounds of the diaphragm and one wound of the inferior vena cava. On admission, 5 patients were in good condition, 2 of these died, 1 lived for one and a half days and died of hemorrhage and another died of peritonitis after seven days. Of 4 patients admitted in fair condition, 3 died, 1 dying on the operating table, another of hemorrhage seventeen hours after operation, and a third of peritonitis six days after the operation. Of 4 patients who were moribund on admission, 3 died of shock and hemorrhage and 1 died of peritonitis three days after the operation. In 9 bodies sixteen wounds overlooked by the surgeon were found at autopsy: seven wounds were in the pancreas, three were in the liver, two were in the left kidney and there was one in the right kidney, stomach, small bowel, and common bile duct respectively. Fat necrosis was noted in 4 of these bodies. In the patients who recovered the stomach was wounded three times, the small bowel two times and the liver and diaphragm each once.

The 6 patients with wounds of the pancreas who did not undergo laparotomy died. All were moribund on admission to the hospital and

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<sup>55</sup> Guleke. Pankreasschuss, *Med Klin* 10 131, 1914.

<sup>56</sup> Wallace, C. A Study of 1,200 Cases of Gunshot Wounds of the Abdomen, *Brit J Surg* 4 679, 1917.

<sup>57</sup> Fraser, J., and Drummond, H. Three Hundred Perforating Wounds of the Abdomen *Brit M J* 1 321, 1917.

underwent laparotomies and whose bodies were subjected to postmortem examination. The belief that many of these patients were severely injured when the operations were performed and were suffering from hemorrhage from shock or from both is supported by these figures. In the 169 bodies (table 12) there were overlooked wounds in 94, in the remaining 75 no overlooked wounds were found.

One factor which played a small but definite part in accounting for the number of bodies with overlooked wounds was the experience of the surgeons. At the Cook County Hospital there have been two resident surgeons for many years. Naturally, they were at hand for these emergency operations. Together they performed laparotomies on 184 patients with bullet wounds of the abdomen. The mortality rate for that group was 57.6 per cent. The mortality rate for 107 patients on whom laparotomies were done by thirty-five other surgeons was 69.1 per cent. In 10 cases the name of the surgeon who performed the operation was not recorded. One of the thirty-five surgeons performed laparotomies on 12 patients, another on 7, three on 6, five on 5, and so on down to the twelve who each performed a single laparotomy.

The influence of experience is also more directly shown by the presence of overlooked wounds in 54.4 per cent of the patients whose operations were performed by the two resident surgeons, whereas the thirty-five other surgeons overlooked wounds in 57.1 per cent of the patients. The difference is small, but the large numbers concerned in the calculations compel some respect for the conclusions. We do not pretend to know all the reasons for the presence in so many bodies of overlooked wounds. Perhaps careful attention to such details in a similar study of the work of any other large urban hospital would disclose corresponding conditions. There were undoubtedly some overlooked wounds in some of the patients who recovered. The exit wound in the back wall of the stomach is not always repaired, and after a time the bullet is removed from the soft tissues of the back.

*The Interval Between the Injury and the Operation (Table 14) —* The importance of a short interval between the injury and the operation gained recognition simultaneously with the importance of laparotomy. Surgeons soon learned that hemorrhage from a fair-sized blood vessel and peritonitis from a leaking intestine accounted for most of the deaths and that both should be repaired as soon as possible. In the earliest tables compiled by Morton,<sup>13</sup> Coley,<sup>65</sup> MacCormac<sup>19</sup> and others<sup>66</sup> attention was called to the value of a short interval between the injury and the operation in lowering the mortality rate, and this was recently reempha-

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<sup>65</sup> Coley, W. B. *Treatment of Penetrating Shot-Wounds of the Abdomen*, Boston M. & S. J. **119** 373, 1888.

<sup>66</sup> See table 1.

of peritonitis three days and seven days after operation, respectively. The bodies of 12 of the 13 patients who died were examined post mortem. In 1 patient, one other viscus besides the spleen was injured, in 3, two others, in 7, three others, and in 1, four others, respectively, were injured, making a total of thirty-two wounds of the viscera in addition to the wounds of the spleen in the 12 patients. There were eleven wounds of the diaphragm and thirty-two additional wounds of the viscera, as follows: of the stomach, ten, of the liver, seven, of the colon, five, of the small bowel, four, of the left lung, four, of the right lung, one, and of the left adrenal gland, one. In 11 of the 12 bodies examined post mortem wounds overlooked or not mentioned by the surgeon were found as follows: three in the spleen, five in the stomach, four in the liver, four in the left lung and one each in the small bowel, left kidney and left adrenal gland, making a total of nineteen overlooked wounds.

The 5 patients not operated on who had wounds of the spleen also had wounds of the thorax and are included in the group of patients with thoraco-abdominal wounds (table 10).

**Wounds Caused by a Single Bullet.** The small number of patients shot with more than one bullet is surprising, for a rapid succession of shots with modern firearms, such as the automatic pistol, may be executed with nearly the same ease as the firing of a single shot. Willis<sup>42</sup> reported the occurrence of wounds from a single bullet in all but 8 of his 58 patients. In our series, 262 of the 301 patients (table 9) who underwent operations had abdominal wounds made by one bullet only, of these, 151 died—a mortality rate of 57.6 per cent. This added trauma to the abdomen by a second or third bullet is pronounced and highly fatal, as shown by the fact that the mortality rate for that group was 85.7 per cent. There is a higher mortality rate, 96.9 per cent, for 22 patients who had abdominal wounds from one bullet and wounds of the extremities by other shots. The 3 patients with wounds of the abdomen made by one bullet and with injury of the thorax by a second died. It is quite obvious that prompt operation and a minimum period of anesthesia are of little avail in cases in which such a multiplicity of wounds is present.

*Thoraco-Abdominal and Abdominothoracic Wounds (Table 10).*—Bullets entering the thorax and passing through the diaphragm into the abdomen or in a reverse direction, from the abdomen into the thorax, produce wounds usually referred to as thoraco-abdominal, although the latter are frequently termed abdominothoracic. Both terms deserve a place because the injuries are likely to be more severe in the first segment of the trunk wounded, the force of the bullet being somewhat expended in the second. Both terms refer to wounds made by a single missile, although the wounds of the thorax and abdomen and their viscera made by a single shot from a shotgun carrying either bird shot or

*Postoperative Drainage (Table 16)*—The question whether laparotomy wounds should be drained and the factors which decide this question have been and still are a subject of controversy among surgeons. The contentions have concerned many conditions other than those due to bullets and have naturally centered about the presence or absence of a grossly evident inflammatory exudate on the peritoneum. This subject of drainage is another detail regarding which the information we possess

TABLE 14—*The Interval between the Injury and the Operation*

Interval (Hours)	Total	Recovered	Died	Mortality (Percentage)
0-2	164	72	92	56.1
2-4	92	29	63	68.4
4-6	8	4	4	50.0
6-9	7	2	5	71.4
9-20	14	4	10	71.0
No data	16	5	11	68.0
Total	301	116	185	61.4

TABLE 15—*Mortality Rate and Duration of Anesthesia*

Length of Anesthesia (Minutes)	Number	Recovered	Died	Mortality (Percentage)
0-30	27	10	17	62.9
30-60	106	43	63	59.4
60-90	95	37	58	61.0
90-120	56	22	34	60.7
120-150	17	4	13	77.0
Total	301	116	185	61.4

TABLE 16—*Relation to the Mortality of (a) Drainage of the Laparotomy Wound and (b) No Drainage*

Management	Total Patients	Recovered	Died	Mortality (Percentage)
With drainage	108	42	66	61.1
Without drainage	87	38	49	56.3
No information	106	36	70	66.0
Total	301	116	185	61.5

is of importance because the number of patients dealt with is larger than usual (table 16). The abdomen was closed with drainage more frequently when the bullet wounded more than a single viscus. Of 108 patients with wounds of only one viscus, drainage was resorted to for only 30. Twenty of the 30 had wounds of either the stomach or bowel, of 182 patients with wounds of two or more viscera the wounds were drained in only 58. Records of the presence or absence of peritonitis or of peritoneal contamination by foreign bodies, feces, etc., at the time of operation unfortunately are too few to be used in attempts to estimate

was learned that the wounds are usually on one side, that the size of the hole in the diaphragm is of great importance, that hernia of abdominal viscera into the thorax occurs chiefly on the left side and that blood

TABLE 10—*Thoraco-Abdominal and Abdominothoracic Wounds in 43 Patients*

Patients with Laparotomies (31)			Patients Without Operations (12)		
Organs Injured	Num ber of Pa tients	Comment	Organs Injured	Num ber of Deaths	Comment
Diaphragm	31	24 died, 7 recovered	Diaphragm	12	All 12 died
Liver	16	were moribund on en	Liver	7	were performed on all
Stomach	16	trance, all were shot	Stomach	4	9 of the 12 were mori
Spleen	10	with one bullet, the	Spleen	5	bund on entrance, all
Left lung	6	average injury, operation	Left lung	3	were shot with one bul
Large blood		interval for those who	Large blood		let, 8 died at an average
vessels	5	recovered was 37 hrs	vessels	2	of 75 hrs after en
Small bowel	4	for those who died it	Small bowel	1	trance, one lived 1 day,
Colon	4	was 48 hrs in 19 of	Colon	1	one 4 days, one 5 days,
Left adrenal		the 23 bodies examined	Left adrenal		and one 13 days
gland	4	after death wounds over	gland	0	
Right kidney	3	looked by the surgeons	Right kidney	0	
Right lung	2	were found	Right lung	3	
Pancreas	2		Pancreas	0	
Spinal cord	1		Spinal cord	1	
Esophagus	0		Esophagus	1	
Left kidney	0		Left kidney	3	

TABLE 11—*The Influence on the Mortality Rate of the Place of Entrance of Bullets and the Direction of Their Paths in Patients Who Had Laparotomies \**

Direction	Upper Part of the Abdomen			Lower Part of the Abdomen			Upper and Lower Parts of the Abdomen			Summary			
	Recoveries	Deaths	Mortality (Percentage)	Recoveries	Deaths	Mortality (Percentage)	Recoveries	Deaths	Mortality (Percentage)	Recoveries	Deaths	Mortality (Percentage)	Total
Front to back	64	92	59 0	24†	42	63 6	0	7	100	88	141	61 5	229
Back to front	12	15	55 5	12‡	16	57 1				24	31	56 3	55
Side to side	3	3	50 0	1	7§	87 5				4	10	71 4	14
Front and side		3	100 0								3	100 0	3
Total	79	113	58 8	37	65	63 6	0	7	100	116	185	61 4	301

\* Among the 92 patients who died from front to back wounds of the upper part of the abdomen 5 were shot in the abdomen with 2 bullets, both bullets had a front to back course

† One patient of the 24 who recovered from bullet wounds of the lower part of the abdomen was shot in that region with 2 bullets passing in from the front

‡ An exceptional recovery occurred in a patient in this group who was shot from behind with 3 bullets

§ Each of the 7 patients who died from wounds of both the upper and the lower parts of the abdomen was shot with two bullets

usually escapes from intrathoracic wounds into the abdomen so that the lungs are not immobilized by hemothorax

*Paths of Bullets (Table 11)*—Of the 301 patients who underwent laparotomies, 229 were shot in front, in 156 of these the wound was in the upper part of the abdomen, in 66 it was in the lower part, and 7 had a bullet in each location—the mortality rates were 59 per cent, 63 6 per cent and 100 per cent, respectively Whether the internal



Of these 17 patients, 16 are included in the 169 who died after laparotomies and whose bodies were examined after death. Eight of the 169 died of miscellaneous causes: bronchopneumonia, spontaneous opening of the laparotomy wound and evisceration, ascending infection of the urinary organs, etc., as set forth in table 17. The patient with the subphrenic abscess was a woman shot with three bullets, one in each upper and one in the lower right abdominal quadrant; death occurred forty-four days after the patient was wounded. The phlegmonous inflammation about the urinary bladder spread, and a generalized peritonitis resulted; there was an unrepaired exit wound, and death occurred fourteen days after entrance.

The pneumothorax followed wounds made by a bullet which entered the left lumbar region, passed through the twelfth thoracic vertebra, left lobe of the liver and diaphragm and lodged in the right seventh intercostal tissues, 2.5 cm. from the sternum; large hemorrhage in the diaphragm and right perirenal tissues occurred; 430 Gm. of blood was present in the right pleural cavity, and there was a huge pneumothorax compressing the right lung.

There was no acute peritonitis associated with the systemic infection due to gas bacilli. Two laparotomy sponges were found in 1 body. After most of the bloody fluid was squeezed out of them, one weighed 28 and the other 83 Gm. That patient's death occurred six hours after operation; the left humerus had been broken by a second bullet; a segment of the ileum was resected, and an unrepaired bullet hole of the sigmoid flexure was found after death.

This death is recorded under the heading of shock and hemorrhage in table 17. Under the heading of acute generalized peritonitis in that table are listed deaths of 2 other patients in whose bodies laparotomy sponges were found after death. One patient died twenty-two hours; the other, one and a half days, after laparotomy. The sponges in these bodies were of the same size, and after most of the fluid they contained had been expressed each sponge weighed 120 Gm. The man who lived one and a half days had two segments of ileum resected, one 12.5 and the other 20 cm. long. The peritonitis was associated with infection due to gas bacilli. In the other body hemoperitoneum from a bullet wound of the left external iliac vein was present; the wound was repaired. Except in the last of the 3 patients, the sponges left in the abdomen probably played no part in bringing about death.

Another death from peritonitis occurred seven days after an operation. A loop of the small bowel 147 cm. distal to the duodenojejunal junction was caught and sutured to the abdominal wall in closing the laparotomy wound. The suture caught the loop opposite the mesenteric attachment. In comments on table 12 some allusion is made to the

of entrance in the right posterior axillary line just above the ninth rib, wounds of the diaphragm and liver, and lodgment of the bullet in the scrotum Both patients recovered

*Overlooked Wounds (Table 12)*—The term "overlooked wounds" has only relative precision, for it undoubtedly is applied here to some wounds which were noted by the surgeons but unmentioned in the hospital record The surgeons were not always present when the post-mortem examinations were made Many of the shootings were criminal, and the necropsies necessarily had a limited audience A pair of unrepaired bullet perforations of a loop of the small bowel found after death has a significance different from that of an overlooked grooving

TABLE 12—*Overlooked Wounds of the Diaphragm and Abdominal Viscera Found at the Postmortem Examination of Patients who Underwent Laparotomies*

	Diaphragm	Colon	Small Bowel	Urinary Bladder	Major Blood Vessels	Left Kidney	Right Kidney	Liver	Left Lung	Stomach	Pancreas	Common Bile Duct	Rectum	Spleen	Left Adrenal Gland	Right Adrenal Gland	Left Ureter
Number of bodies with overlooked wounds of one viscus	2	13*	10	6	6	5	4	3	3	1	1	0	1	1	1	0	0
Number of bodies with overlooked wounds of more than one viscus†	13	10	6	3	11	7	5	11	8	7	6	1	2	3	3	2	1
Total number of overlooked wounds of each viscus	15	35	22	11	18	12	9	14	11	9	7	1	4	4	4	2	1

\* In one body of this group of 13 there were also 2 laparotomy sponges

† The figures in this row are overlapping For example if there were 10 bodies with overlooked wounds of the colon and in the same bodies overlooked wounds of other viscera these 10 bodies are counted in other places in this row A body with overlooked wounds in the colon and small bowel has a place in the vertical columns for each viscus it is counted twice There were overlooked wounds of the colon in 23 bodies but in some bodies the wounds numbered 2 or more totaling altogether 35 wounds in 23 bodies The overlooked wounds numbered 164 in 94 bodies in 55 bodies there were overlooked wounds of a single viscus, and in 39 bodies there were overlooked wounds of two or more viscera

perforating wound made by a bullet in the back wall of the colon close to the spleen This difference acquires greater significance when the pair of in and out unrepaired perforations made by a bullet in a loop of the small bowel are associated with many other repaired perforations in other loops

One may not be surprised to find overlooked wounds when patients die on the operating table In the bodies of 11 of the 13 patients who died under such circumstances there were wounds unmentioned in the hospital records When some of the necropsies were made not all of the observations by the clinicians had been entered on the records accompanying the body to the morgue In addition to the 13 patients who died on the operating table, 87 others died during the first twenty-four hours after laparotomy, making a total of 100 of the 169 (table 4) who

was placed against the trunk, the exit wound for one of the two matched a third entrance wound in the left side of the chest. The bullet entering there broke the lower margin of the tenth rib, passed through the diaphragm, spleen and left kidney and entered the aorta.

A few hours after the shooting the left leg became paralyzed, and severe pain occurred throughout the left foot. The bullet was removed from the left femoral artery by Dr. Karl Meyer. It had lodged near the groin and the peritoneal cavity was not entered in the process of removing the bullet. Laparotomy was not performed. Gangrene of the left lower extremity was followed by amputation of that extremity. Death occurred four days after entrance. At the necropsy 732 Gm of blood was found in the left pleural cavity, only 24 Gm was present in the abdomen. The entrance wound in the aorta was 8 mm in diameter and had inverted edges, it was located 4 mm cephalad to the mouth of the left renal artery. Just to the right of the mouth of the celiac axis the aorta bore a triangular tear 12 by 3 mm, with everted edges. The periaortic fat there was intact. There were no clots in or about the aortic wounds. In the periaortic fat from the seventh thoracic vertebra down and about all the abdominal portion of the aorta there was a marked retroperitoneal hemorrhage. That the patient lived four days with such wounds in the aorta was as astounding as the migration path of the bullet.

Rubesch<sup>71</sup> found accounts in medical literature of the migration of missiles in the heart and blood vessels in 16 persons, to these reports he added 1. In 4 patients migration was from the heart. In one of these, his own patient, the bullet lodged in the right femoral artery, amputation was followed by recovery. In 3 other patients the passage of the missile probably occurred post mortem. Eleven patients who had no operations and 3 who had, all died, 4 recovered.

In our series bullet wounds of the aorta were found after death in the bodies of 7 patients who had not undergone laparotomy and in 2 of those who had, these last died on the operating table, the 7 who had not undergone laparotomy died from fifteen minutes to one hour after entrance except the patient with the bullet lodged in the femoral artery, who lived four days. Momm<sup>72</sup> reported the occurrence of a death twenty-seven days after the abdomen was wounded by a bullet which injured the liver and aorta. On account of a massive hemorrhage in the abdomen the wound in the liver was packed. Gangrene of the left leg developed, about a week before death an aneurysm of the left femoral artery in the groin was opened and the bullet was found between

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71 Rubesch R. Ein Beitrag zur embolischen Verschleppung von Projektilen, *Beitr. z. klin. Chir.* 60:394, 1912.

72 Momm. Ein Schuss durch Leber und Aorta, Tod nach vier Wochen infolge Sepsis, *Deutsche med. Wchnschr.* 36:2242, 1910.

sized by Lewis <sup>67</sup> Of the 30 cases recorded in the table by MacCormac, for example, the average interval between the injury and the operation for patients recovering was eight hours and for those dying, twenty-one hours The same relationship obtains in many subsequent reports except that the interval for both those recovering and those dying has been shortened For the 17 of the 23 patients in Marks' <sup>68</sup> series who recovered the average interval was three and seven-tenths hours, and for those dying, five and six-tenths hours Prev and Foster <sup>69</sup> reported even shorter periods for their 22 patients, one and eighty-eight hundredths hours for those recovering, and three and four-tenths hours for those dying

For most of the patients in our series the interval was short Over 77 per cent of the patients were operated on within three hours after injury and the mortality rate for that group was 60 per cent, for those who were operated on after three hours the mortality rate was 65 per cent The proximity to and availability of competent hospital and

TABLE 13—*Mortality Rate, Condition on Admission and Laparotomies*

Condition	Number	Recovered	Died	Mortality (Percentage)
Good	66	46	20	30.3
Fair	123	55	68	55.3
Poor	112	15	97	86.6
Total	301	116	185	61.4

surgical care in large cities usually provide a short interval between the injury and the operation Naturally, some long intervals are due to prolonged clinical observations

*Anesthesia*—Apparently the influence of anesthesia is not evident unless it is prolonged (table 15) The high mortality rate for the 27 patients anesthetized for thirty minutes or less was due to their critical condition Some died on the operating table soon after the operation was begun With few exceptions the anesthetic used was ether The average time of anesthesia for the patients who recovered was seventy-one and six-tenths minutes, for those who died it was seventy-six minutes One patient who died had only a local anesthetic

<sup>67</sup> Lewis, Dean, in discussion on Lewis, Dean, and Trumble, I Ridgeway Subcutaneous Injuries of the Abdomen, *Ann Surg* **98** 685, 1933

<sup>68</sup> Marks, H Penetrating Gun-Shot Wounds of the Abdomen, *Tr M A Missouri*, 1893 p 324, Gunshot Wounds of the Stomach, Laparotomy, Death, *St Louis Courier Med* **11** 11, 1894, Operations on Gunshot Wounds of the Abdomen, *ibid* **12** 14 and 41, 1895

<sup>69</sup> Prev, D, and Foster, J M Gunshot Wounds of the Abdomen, *Ann Surg* **99** 265, 1934

Thoraco-abdominal and abdominothoracic wounds are associated with a high mortality rate

Overlooked wounds also play a large part in the mortality. Unfortunately, however, their influence is malign and the study of their importance has been neglected.

Patients who die of bullet wounds in the first twenty-four hours after injury die of hemorrhage and shock, when death occurs after twenty-four hours it is usually due to generalized peritonitis.

In only a few patients do the wounds require resection of viscera or parts of viscera.

the part played by drainage or its absence on mortality. Apparently drainage did not have a large influence on the mortality.

*Causes of Death (Tables 17 and 18)*—The severity of the injuries and the operations required both contributed to the mortality rate of

TABLE 17—Data on 205 Necropsies

Patients with Laparotomies (169)	Number with Over looked Wounds	Number with No Over looked Wounds	Totals	Patients with No Laparot- omies (36)	Totals
Acute generalized peritonitis	45	46	91	4	95
Shock and hemorrhage	41	26	67	1	101
Bronchopneumonia	2	0	2	0	2
Spontaneous evisceration	1	0	1	0	1
Systemic infection with gas bacilli	0	1	1	1	2
Ascending inflammation of the urinary organs	1	0	1	0	1
Phlegmonous inflammation about the urinary bladder	1	0	1	0	1
Pneumothorax on right side	0	1	1	0	1
Subphrenic abscess	0	1	1	0	1
Totals	91	75	169	56	205

TABLE 18—Bullet Wounds of Blood Vessels and Concomitant Visceral Injuries

Injured Blood Vessels	Data on the 24 Patients with Laparotomy and Injuries to the Blood Vessels with Associated Visceral Injuries												Data on the 17 Patients with No Operations, with Injuries to the Blood Vessels and Associated Visceral Injuries													
	Small Bowel	Liver	Stomach	Pancreas	Urinary Bladder	Left Kidney	Colon	Common Bile Duct	Left Adrenal Gland	Left Lung	Spinal Cord	Total	Small Bowel	Liver	Stomach	Pancreas	Urinary Bladder	Left Kidney	Right Kidney	Colon	Spleen	Jejunum	Left Lung	Right Lung	Total	Grand Total
Inferior vena cava	4	1	4	3	0	0	2	1	0	0	0	8	1	1	1	0	0	0	0	0	0	0	0	0	2	10
Iliac blood vessels	4	0	1	0	1	0	0	0	0	1	1	5	3	0	1	0	3	0	0	0	0	0	0	0	5	10
Aorta	1	2	1	0	0	0	0	0	0	0	0	2	1	5	2	2	0	2	0	1	1	1	1	0	7*	9*
Mesenteric blood vessels	3	4	1	0	0	1	1	0	1	0	0	7	0	0	0	0	0	0	0	0	0	0	0	0	0	7
Renal blood vessels	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	0	0	0	0	0	0	0	1*	2*
Left femoral vein	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1
Right subclavian ar- tery	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	1	1
Left internal pudic artery	1	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Splenic vein	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	1	0	0	0	0	0	0	1*	1*
Heart	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	1	1	1	1
Total	13	7	8	3	2	1	3	1	1	1	1	24	6	10	7	4	3	4	1	1	1	1	2	2	17	41

\* One patient had wounds of the aorta, the splenic and left renal veins and had no laparotomy. In the remaining 40 one large blood vessel was wounded.

69.1 per cent for resections in 23 patients. In 1 patient resection of the spleen, in 2 patients, of the gallbladder, in 3 patients, of portions of the jejunum, in 4 patients, of one kidney, and in 13 patients, of segments of the ileum, was performed. Seven of the 23 patients recovered. In 17 of the 23 there were wounds in places other than the parts removed.

pital and the Cook County Hospital are shown graphically (fig 1). The number of cases before 1916 was high. The sharp decline in the incidence began a year earlier in Minneapolis than in Chicago. A study of the death rate in the registration area of the continental United States also gives the impression that the use of liquor is a factor in the production of the disease. In figure 2 is shown the decrease in the number of deaths due to cirrhosis after state and federal prohibition laws went into effect. A graph based on the figures obtained from Stockholm, Sweden, is shown for comparison. The great difference

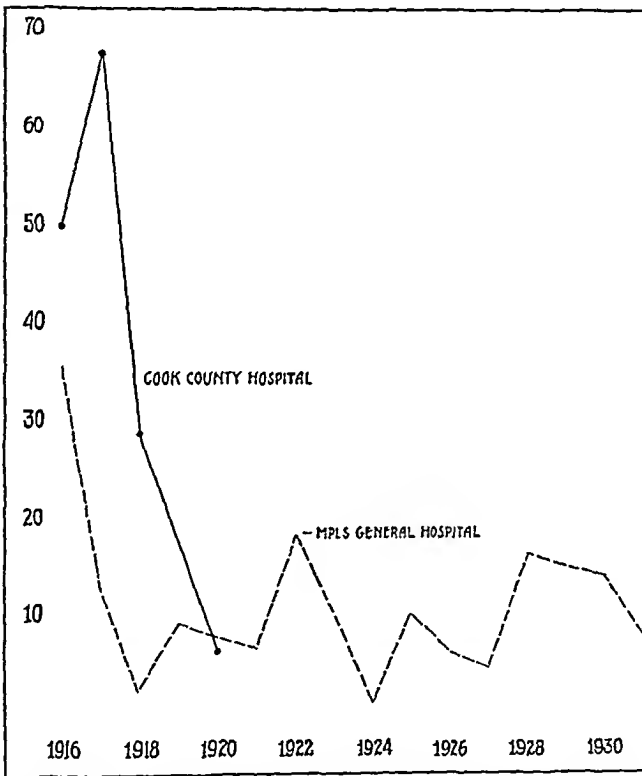


Fig 1—Graphs showing the number of patients per ten thousand of the population discharged who had a condition diagnosed as cirrhosis of the liver from the Minneapolis General Hospital from 1916 to 1932 and from the Cook County Hospital from 1916 to 1920.

between the curve for Minnesota (largely rural) and those for such states as New York and California (largely urban) may be due to the infrequency of diagnosis in rural districts or to the greater frequency of the condition in the urban population. Differences in diet, drinking habits and disease may be factors.

O'Malley stated that in certain classes of Orientals who never use alcohol but do use spices and other stimulating articles in their diet

part overlooked wounds have in causing peritonitis. We believe that such wounds occurring in the colon deserve a high place in any consideration of the dangers resulting from overlooked wounds.

We found in some records that the surgeons had mentioned the presence of feces in the abdomen or of foreign material such as cartridge wadding or fragments of cloth. But such observations were seldom mentioned, and the absence of such soiling of the peritoneum was not included in the protocols, from such sources the cause of the peritonitis remains unexplained. The figure for deaths resulting from peritonitis (91) and those for death resulting from hemorrhage and shock (70) are only approximate (table 17). The surgeons and the pathologist noted that some bleeding had taken place from wounds of patients in whom peritonitis subsequently developed. An added difficulty is the presence of overlooked wounds in about one half of these 161 bodies. It is impossible to assign each death to any single definite cause.

The most conclusive results were obtained in cases in which death was known to be due to hemorrhage. It will be recalled that of the 343 patients in our series, 42 had no operations, and that of these, 37 died and only 1 was not examined at necropsy. Naturally, deaths from bleeding would be regarded as the reason for failure to explore the abdomen of these 42 patients and attempt repair of the wounds. In the postmortem examinations of 36 of these 42 bodies, evidence of severe hemorrhage was found in 17<sup>70</sup> (table 18). Just how many of these patients would have recovered after laparotomy and ligation of the bleeding vessels is speculation, but Lewis<sup>67</sup> stated that when it is a question of shock or hemorrhage he would first control the hemorrhage and then give a transfusion. The aorta was wounded in 7, the left common iliac artery in 3, the inferior vena cava in 2 and the left internal iliac vein, the left external iliac vein, the left femoral artery, the right subclavian artery, the left renal vein, the splenic vein, and the heart each in 1 body.

Sixteen of the 17 patients arrived moribund, 10 were shot with one bullet, 6 with two, and 1 with three. In the patient shot with three, all three bullets entered in front, causing wounds of the aorta, left renal vein and splenic vein as well as of the stomach, liver, pancreas and left kidney. In the others (16) only one large blood vessel was wounded in 15, in 1 the heart was injured. Sixteen of the 17 patients lived for an average of two and three-tenths hours after entrance, the seventeenth lived for four days. This was a middle-aged man shot by his son there were entrance and exit wounds in the upper part of the left arm, with bullet paths connecting the wounds for two bullets. When the arm

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<sup>70</sup> Under "General Considerations," p 392, the causes of death for the remaining 19 patients are reviewed, 5 of the 42 who had no operation recovered.



## DIAGNOSIS

The main object of the study reported here was to show what results can be expected from the surgical treatment of cirrhosis of the liver. In order to do this the literature on the subject was studied, and the records were reviewed of cases in the Minneapolis General Hospital and the University of Minnesota General Hospitals in which a diagnosis of cirrhosis had been made. Several of the charts recorded the diagnosis of Banti's disease or splenic anemia in addition to that of cirrhosis.

Of the 241 cases listed as instances of cirrhosis of the liver, 5 were included instead with those of splenic anemia, and 64 were excluded

TABLE 1—*Summary of Cases in Which the Diagnosis Was Cirrhosis of the Liver\**

	Number
Cases in which the diagnosis was cirrhosis	241
Excluded to be classified as cases of splenic anemia	5
Excluded after inspection of liver at autopsy	5
Excluded after examination of microscopic sections	10
Excluded because the diagnosis was questionable	64
Total cases excluded	79
Cases remaining for study	162
Cases in which the probable diagnosis was cirrhosis though not verified at autopsy or by biopsy	78
Cases in which the diagnosis was certain	84
Verified at autopsy	67
Verified at operation and by biopsy	17
Diagnosis made clinically	49
Diagnosis not made clinically	35
Patients known to be alive	3
Patients known to be dead	80
Condition unknown	1
Cases in which operation was performed	31
Talma Morison (omentopexy, epiploexy)	9
Talma Morison and splenectomy	4
Splenectomy	4
Exploratory operation*	10
Cholecystotomy*	1
Cholecystogastrostomy*	1
Cholecystoduodenostomy*	1
Ventral herniotomy*	1

\* The diagnosis of cirrhosis of the liver was not made until at operation or autopsy in most of these cases.

because the diagnosis was questionable owing to the presence of cardiac or renal disease, ulcers or congenital hemolytic icterus (table 1). That the symptoms in cases of cirrhosis may closely simulate those of these conditions will be seen from a study of the symptoms and findings given later. Cases were therefore probably excluded which rightfully should not have been. In 5 of 10 other cases which were excluded the clinical diagnosis was not confirmed on gross examination at autopsy, and 5 in which the diagnosis based on the gross appearance at postmortem examination was cirrhosis were excluded after microscopic examination by Dr J. S. McCartney of the department of pathology of the University of Minnesota. He has recently completed a study of the

the artery and vein where pulsation had so pounded the bullet against the artery that the wall was torn for a length of 3 cm. After death a hole 7 by 3 mm in diameter was found in the front wall of the aorta, 12.5 cm above its bifurcation. On the opposite side was a hole 6 mm in diameter through only the intima and media.

Without describing the entrance wound in the aorta, Kratter<sup>73</sup> has registered migration in the aorta of a bullet to a straddlewise lodging at the aortic bifurcation, obstruction of the left common iliac artery, gangrene of the left leg, amputation, death from uremia and ascending inflammation of the urinary organs in a woman who attempted suicide, laparotomy disclosed no visceral injury, death occurred two months after the shooting. Brentano<sup>74</sup> had a patient who lived for one week with two holes in the aorta where a 7 mm bullet had passed from left to right close to the mouth of the superior mesenteric artery, its path being completely retroperitoneal. The review by Perthes<sup>75</sup> of the older literature includes 7 cases in which patients lived for from six to sixty days after sustaining bullet wounds of the aorta, one in which the patient lived for seven weeks and that of his own patient, who lived two hundred and ninety-five days.

#### CONCLUSIONS

The introduction of laparotomy for bullet wounds of the abdomen is definitely an American contribution to surgery, particularly by surgeons of the southern states.

Perhaps the most important element aiding the recovery of patients with bullet wounds of the abdomen is a short interval between the injury and the operation. This was recognized many years ago, and the discovery initiated a mortality rate that has not been appreciably changed since. It is common knowledge, however, that the publication of recoveries has met with more favor than that of deaths, whether the reports concern 1 or many patients.

The experience surgeons have had in dealing with this type of injury undoubtedly is a helpful factor.

Drainage after laparotomy for bullet wounds apparently is unimportant.

Bullet wounds of the abdomen in peace time occur especially in persons in the third decade of life in the period of youth and daring.

Bullets entering the front of the abdomen cause more deaths than those entering the back, those entering the sides cause most deaths.

<sup>73</sup> Kratter. Seltene Schussverletzungen, *Vrtiljschr f gerichtl Med* **31** 342, 1906.

<sup>74</sup> Brentano. Schussverletzung der Aorta, *Verhandlung d deutsch Gesellsch f Chir* **33** 92, 1904.

<sup>75</sup> Perthes, G. Schussverletzung der Arteria pulmonalis und Aorta, *Beitr z klin Chir* **19** 414, 1897.

## SEX AND AGE

As can be seen from table 2, cases occurring in men predominate in the proportion of about 3 to 1. The average age for both sexes is 49.5. The average age of the men is 50.5, and that of the women, 45.1. In figure 3 is shown the number of patients for each five year period of life. The disease is most common in the fourth and fifth decades.

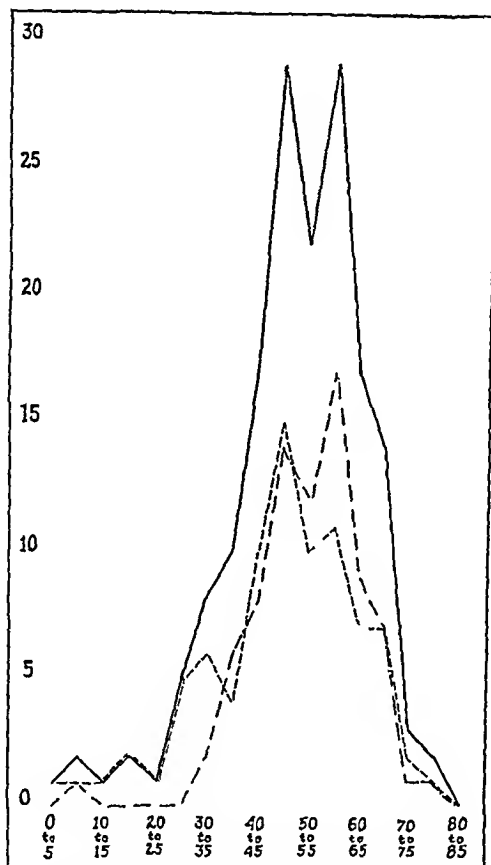


Fig. 3.—Graphs showing the distribution of cases according to age. In this figure the values for patients with proved cirrhosis are shown by short dashes, those for patients with probable cirrhosis, by a line of dots and dashes, and those for all patients by a solid line.

## SYMPTOMS

Table 3 shows that the most common single complaint was that of abdominal distention (in 101 of 162 cases). It was usually due to ascites, but it may also be caused by an enlarged liver or spleen or by gaseous distention of the intestines.

In a study of 5,000 cases of ascites Cabot found that a correct diagnosis was made in only 39 per cent. The following causes were given in the order of their frequency: cardiac involvement, 1,397 cases,

# CIRRHOSIS OF THE LIVER

WITH SPECIAL REFERENCE TO THE SURGICAL ASPECTS

EARL CLIFFORD HENRIKSON, M D

MINNEAPOLIS

Laennec, in 1819, was the first to describe adequately and to name portal cirrhosis. Since his time hundreds of papers have been written, and many types of cirrhosis have been described. The following classification used in this study is taken from Bell's "Text-book of Pathology"

- 1 Portal cirrhosis (Laennec's cirrhosis, atrophic cirrhosis, hobnail liver or gin-drinkers' liver)
- 2 Obstructive biliary cirrhosis
- 3 Pigmentary cirrhosis (hemochromatosis, bronze diabetes)
- 4 Syphilitic cirrhosis

Before discussion of the treatment of cirrhosis of the liver, which for years has been directed mainly toward relief of the ascites associated with the condition, the etiology, diagnosis, symptoms, physical findings, postmortem observations and causes of death will be considered.

## ETIOLOGY

The etiology of cirrhosis is obscure. The importance of alcohol as a factor becomes less and less convincing as the results of postmortem examination in large series of patients dying of alcoholism are studied. There was a history of the use of alcohol to some extent in 50 per cent of the cases considered in this paper. In many of the hospital records there is no indication whether the patient was asked about the use of alcohol. Many patients known to use liquor refuse to admit it. These facts are offset by the impression that an equally high percentage of patients with no cirrhosis will admit the use of alcohol. Formad observed cirrhosis at only 6 of 250 autopsies performed on chronic drunkards. However, the marked decrease after 1916 in the number of patients admitted to hospitals with a condition diagnosed as portal cirrhosis would seem to prove some association. To illustrate, the statistics compiled from the records of the Minneapolis General Hos-

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peritonitis, in others. One of the more likely theories is that which explains the ascites as due to the circulation of toxins which the liver is unable to handle as a result of the great changes in it. This theory is favored by the presence of edema prior to the ascites. These toxins are said to arise from both the gastro-intestinal tract and the spleen. The latter organ may enlarge enormously and be responsible for as much as 50 per cent of the blood passing through the portal vein.

If one considers as most likely the theory that ascites is due to a combination of toxemia and portal obstruction, any operative procedure should aim (1) to relieve portal obstruction, as by the establishment of a collateral circulation, (2) to aid the liver in dealing more satisfactorily with the toxins, as by lessening the portal congestion and increasing the arterial supply to the hepatic cells, thus allowing hyper-

TABLE 3—*Frequency of Occurrence of Symptoms in 162 Cases of Cirrhosis*

Symptoms	Proved Cirrhosis	Probable Cirrhosis	Proved and Probable Cirrhosis
Gastro intestinal	65	61	126
Abdominal pain or distress	37	44	81
Nausea and vomiting	23	21	44
Constipation	12	18	30
Anorexia	19	19	38
Hematemesis	20	18	38
Bloody or tarry stools	16	11	27
Diarrhea	9	9	18
Clay colored stools	4	4	8
Abdominal distention	45	56	101
Weakness	30	31	61
Loss of weight	26	30	56
Swelling of the feet	27	28	55
Dyspnea	24	30	54
Nocturia	22	26	48
Jaundice	26	21	47
Cough	9	12	21

plasia to take place, and (3) to remove the source of toxins when possible. If the spleen really is such a source, splenectomy would be of benefit, not alone because a source of toxins is eliminated but because the portal trunk is relieved of from 20 to 50 per cent of its venous blood supply.

Gastro-intestinal symptoms, present in 126 of 162 cases, may all be more or less dependent on the stasis in the portal vein. Hematemesis (present in 38 of 162 cases) may be due to (1) ulceration and rupture of dilated vessels at the lower end of the esophagus, (2) erosions and necrosis of the mucosa as a result of infective processes or (3) congestion of the gastric mucosa. In a study of 411 cases of gastro-intestinal hemorrhage Rivers, at the Mayo Clinic, determined that in 90 per cent the hemorrhage was due to intrinsic gastroduodenal lesions, such as peptic ulcer (in 78 per cent) and carcinoma of the stomach (in 78 per cent). Extrinsic lesions, such as cirrhosis of the liver (in 28 per cent) and splenic anemia (in 28 per cent) were responsible for the hemorrhage in 10 per cent of the cases. In respect to the two con-

cirrhosis of the liver is common. This observation adds weight to the theory that the disease may have a gastro-intestinal origin. One such hypothesis is that portal cirrhosis is caused by toxins or toxin-producing agents brought to the liver by the portal system and that if these toxins are carried by the arteries the disease may resemble the biliary types. Italian pathologists incline to the opinion that toxins arising in the spleen induce the disorder. Other foreign investigators believe that malaria is a factor, but few, if any Americans accept the malarial variety. Cirrhosis has been produced experimentally in animals by chloroform or a similar agent combined with bacterial infection and also by repeated injections of egg white or other protein to produce

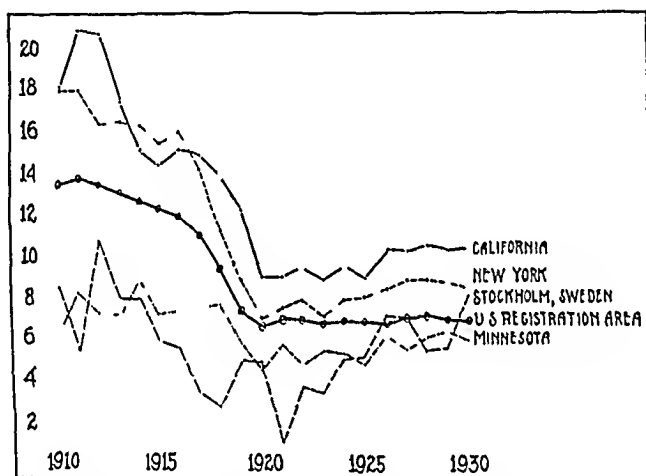


Fig. 2—Graph showing the death rate due to cirrhosis of the liver per hundred thousand of the estimated population of the registration area of the United States from 1910 to 1930. The other graphs indicate that the diagnosis is made much more frequently in California and New York than in Minnesota. A graph constructed from the statistics obtained from Stockholm, Sweden, shows the same general trend as those for the three states selected as samples.

anaphylactic shock. Arsenic and copper are often accused. Hard liquors are said to be more likely than wine and beer to cause the condition. It would be interesting to know definitely whether there is any relationship to the use of alcoholic drinks before or after meals and whether the liver protected by the previous ingestion of carbohydrates is as readily injured as one not so protected. The coexistence of cirrhosis and diabetes, as in cases of bronze diabetes, at first thought seems to indicate that carbohydrates are of no value. However, in such cases diabetes may be superimposed on cirrhosis already well under way, or the same process may involve not only the liver and spleen but the pancreas.

Weakness (in 61 of 162 cases), dyspnea (in 54 of 162 cases), debility, palpitation and irregularities of menstruation may be explained on the basis of anemia and less often on that of cardiac involvement. Loss of weight (in 56 of 162 cases) may be dependent on the gastrointestinal symptoms, but Hollins, who expressed the belief that *Bacillus coli* is the cause of splenic anemia (Adam suggested it as a cause of hepatic cirrhosis), considered the wasting to be a result of the effect of toxins on the central nervous system. He stated that there is vasomotor paresis of the splanchnic area. Hebetude, nervousness, restlessness and insomnia, which were rare in this series, are attributed to toxemia due to a poorly functioning liver.

TABLE 4—*Frequency of Occurrence of Physical Findings in 162 Cases of Cirrhosis*

	Proved Cirrhosis	Probable Cirrhosis	Proved and Prob- able Cirrhosis
Abdominal distention	65	56	121
Ascites	57	52	109
Palpable liver	53	48	101
Cardiac murmur	39	40	79
Edema	38	33	71
Jaundice	22	32	54
Abdominal varices	21	27	48
Palpable spleen	23	24	47
Enlarged heart	29	17	46
Hernia	14	12	26
Dyspnea	13	10	23
Cyanosis	16	7	23
Hemorrhoids	5	6	11
Blood pressure average	118 systolic, 73 diastolic	123 systolic, 75 diastolic	120 systolic, 74 diastolic
Systolic, above 140	9 of 70	11 of 57	20 of 127
Systolic below 120	40 of 70	21 of 57	61 of 127

#### PHYSICAL FINDINGS

The most common physical finding is ascites (observed in 121 of the 162 cases, table 4). This condition has already been considered in detail. A palpable liver, present in 101 cases, was the next most frequent finding. Some investigators consider hypertrophy of the liver as merely one stage of cirrhosis, while others differentiate the atrophic and the hypertrophic type. A palpable spleen was found in 47 of the 162 cases. The enlargement may be due to obstruction of the hepatic and portal circulation or to the fact that the spleen is equally involved by the process producing the disease picture. The symptom complex known as Banti's disease may represent one extreme of a pathologic process which at one time affects the liver more severely and at another the spleen.

Cardiac murmur, which occurred in a large number (79) of the 162 cases in this series, edema (in 71), cardiac enlargement (in 46) and cyanosis (in 23) may serve to confuse the diagnosis of cirrhosis.

microscopic sections of the liver in about 300 cases of cirrhosis, taken from the autopsy material of that department. He examined the sections available in the series of cases considered in this paper. Seventy-eight of the 162 remaining cases were classified as instances of probable cirrhosis. While the symptoms and physical findings in these cases were typical, the liver was not examined, either grossly or microscopically, to confirm the diagnosis. In 84 cases the diagnosis of cirrhosis was verified. In 67 of the latter cases the diagnosis was verified by a study of autopsy material and in 17 by examination or biopsy at operation. In only 3 of the 84 proved cases are the patients known to be alive, the condition of 1 patient is unknown, and the rest are dead.

An examination of table 2 shows that of the group of proved cases 64 were classed as instances of portal cirrhosis, 7, of the obstructive

TABLE 2—*Distribution of Cases of Cirrhosis*

	Proved Cirrhosis	Probable Cirrhosis	Proved and Prob- able Cirrhosis
Number of cases	84	78	162
Types of cirrhosis (based on clinical diagnosis)			
Portal	64	48	112
Biliary (obstructive)	7	3	10
Syphilitic	7	8	15
Undefined	6	19	25
Sex			
Men	61	63	124
Women	23	15	38
Average age, years	47.5	52.1	49.5
Men	49.2	51.9	50.5
Women	40.9	52.7	45.1

biliary type, and 7, of the syphilitic type, while in 6 instances the diagnosis of cirrhosis was unqualified. The distribution according to these types was 48, 3, 8 and 19, respectively, for the group of probable or clinical cases. In 49 of the 84 proved cases the diagnosis was made clinically.

The diagnosis of cirrhosis of the liver is not always easily made, and in a few cases, as has just been mentioned, even gross examination of the liver may be misleading. Without question, many cases are reported in the literature as instances of cirrhosis in which the diagnosis would not be confirmed if sections of the liver were examined microscopically. If results obtained with the various types of treatment are to be compared to determine which method is the best, only cases proved to be instances of cirrhosis at autopsy or by biopsy should be included in the study. From the tables included in this paper a comparison can be made between the proved and the probable cases. The diagnosis in all cases in which it was not verified by autopsy or biopsy is based on the symptoms, physical and laboratory findings and apparent cause of death.



the count in the probable cases being 6,060 and that in the proved cases, 6,380. The count was below 7,000 in 65 of 113 cases (57 per cent).

The urea nitrogen content of the blood averaged 19.4 mg for 23 probable cases and 25.4 mg for 35 proved cases. The average for 58 cases of the two groups in which it was determined was 23 mg. In 16 cases in which an operation was performed the urea nitrogen content ranged from 2.4 to 101 mg (table 5). The patient with a content of 2.4 mg died on the second day after an operation for a ventral hernia. The patient with the reading of 101 mg had had a value of 35 mg a short time previously. She died about one and one-half years after a Talma-Morison procedure.

Tests of hepatic function were performed in only a small percentage of the cases in this series. The pheno-tetra-chlorophthalein test was usually employed, and in 16 of 19 tests impaired function was demonstrated. Rowntree found some degree of retention of bromsulphalein in 80 of 87 patients in his series of 112. Barker expressed the belief that the rose bengal test is the best. The normal person retains 50 per cent of this dye for the first eight minutes and 25 per cent for sixteen minutes, while the person with cirrhosis retains from 65 to 85 per cent for eight minutes and from 40 to 75 per cent for sixteen minutes.

The results of Wassermann tests of the blood, urinalyses, Ewald tests, fractional determinations and analyses of the stools are shown in table 5.

The ascitic fluid in a typical case of cirrhosis is clear and yellowish or greenish and may have a specific gravity as high as 1.015, it contains as much as 0.4 per cent albumin. More albumin is present in cases of cirrhosis than in those of renal ascites and less than in those of cardiac and tuberculous ascites. In the latter condition the specific gravity is about 1.020, the fluid is turbid, and the predominating cell type is the lymphocyte. In cirrhosis the endothelial cell predominates. The presence of polymorphonuclear leukocytes indicates peritonitis.

#### OBSERVATIONS AT AUTOPSY

Autopsy was performed on 67 of the patients in this series. The spleen was removed at operation in 8 cases. The data were incomplete in a few instances. The average weight of 61 livers was 1,760 Gm. (A liver weighing 525 Gm. from a child 8 years old and another weighing 625 Gm. from a child 1 year old are not included.) The usual normal limits for the weight of the liver of an adult ranged from 1,300 to 1,800 Gm. The largest liver in this series weighed 3,200 Gm. Four weighed more than 3,000 Gm. Twenty-one weighed more than 2,000 Gm. The smallest liver weighed 550 Gm., 26 weighed less than 1,500 Gm., and 9 less than 1,000 Gm.

renal damage, 665, cirrhosis, 325, tuberculous peritonitis, 263, ovarian and uterine tumors, 118, abdominal carcinoma, 109, and intestinal obstruction, 86 In 7 per cent of these cases ascites observed at autopsy proved to be due to cirrhosis of the liver Some investigators believe that in most cases ascites associated with cirrhosis is caused by tuberculous peritonitis Tuberculosis may be an incidental observation, however

A commonly considered cause of ascites is obstruction of the portal circulation, resulting from contraction of fibrous tissue about the blood vessels or from portal thrombosis, which is frequently found associated with cirrhosis and especially with splenic anemia Warthin expressed the belief that splenomegaly and the symptoms of Banti's disease are all due to primary infective thrombophlebitis of the portal or splenic veins and that when the condition is present in the portal trunk ascites develops, while if the splenic vein is blocked hematemesis may result from the rupture of dilated branches of the gastric veins When the superior mesenteric veins are occluded pain, vomiting and diarrhea develop, and the patient collapses Against the view that the fibrotic liver causes the obstruction are the many recorded cases of cirrhosis in which death occurred without ascites (65.6 per cent of a series of 56 cases reported by Lange at Kiel, Prussia, in 1888) A well established collateral circulation may have been present in many of these cases In spite of the fact that ascites is the most common finding in cases of portal thrombosis (40 of 61 instances collected by Rolleston), the observation that the portal vein may be ligated in animals without the production of ascites is against the theory of portal obstruction as a common cause Furthermore, in cases of thrombosis of the portal vein immediate effusion into the peritoneal cavity does not always take place, according to Ketchen Then, too, in cases of atrophic cirrhosis considerable pressure on the portal vein exists before ascites supervenes This is shown by the fact that hemorrhages occur long before fluid is present If the fluid were a transudate from the blood vessels, the effusion would pass into the bowel and stomach and not into the peritoneal cavity, as it is in the mucous membranes rather than in the peritoneum that increased blood pressure resulting from occlusion of the portal vein produces the most marked engorgement

Other theories attribute the ascites to the secretory activity of the endothelium, to increased inflow of lymph, to increased permeability of the walls of the blood vessels due to congestion or inflammation, to decreased outflow from the peritoneal cavity because of the obliteration of efferent vessels or to the decreased absorptive power of the endothelium and blood vessels, such as is seen in cases of chronic passive congestion Cardiac failure may be important in some cases, chronic

ascites in a few hours With further repetition of the injury to the liver with carbon tetra-chloride ascites developed which could not be controlled by diet

Hepatic insufficiency is treated by pushing the administration of carbohydrates intravenously and orally Digestive disturbances should be treated symptomatically Complications are treated as they arise Mercury and iodides may be tried, but if improvement results the possibility of wrong diagnosis presents itself For itching Rowntree advised from  $\frac{1}{4}$  or  $\frac{1}{2}$  grain (16.2 or 32.4 mg) to as high as 2 grains (129.6 mg) of mild mercurous chloride daily for three or four days at a time Sweating may bring relief

The dietary restrictions usually observed are as follows Alcohol, eggs, spices, condiments and fats are forbidden The staple article of diet should be milk This is supplemented by vegetables, cooked fruits, cereals and bread Meats are allowed only occasionally

To deplete the circulation mild saline cathartics, such as solutions of sodium phosphate, magnesium citrate and magnesium sulfate, are said to be useful Blum, Aubel and Hausknecht described 3 cases in which calcium chloride with restriction of salt (sodium chloride) was used with good results The dose is from 11.1 to 22 Gm by mouth for from five to six days at intervals of from eight to ten days The calcium is eliminated by the bowel, the chlorine, by the kidney As the chlorine is freed from the calcium it is forced to combine with the sodium, and the sodium is eliminated and with it the surplus of water Further work with calcium chloride has been done by Mejebovskiy, who studied 11 patients on a diet of baked potatoes, rice cooked without salt, boiled meat, fruit and eggs One or two glasses of weak tea were allowed daily For two or three weeks from 12 to 15 Gm of calcium chloride was given daily, and this was well tolerated The results were positive in 8 cases and negative in 2, and the degree of ascites remained stationary in 1 instance Recurrences developed in 6 cases after from three to eleven months In 1 case the amount of urine increased fourfold The sodium chloride content increased notably in the urine and blood One patient lost 15 Kg in weight in three weeks The ascites disappeared The loss of weight was not associated with diuresis, since the intake of fluid was 500 cc, and the output of urine, only 400 cc Calcium chloride would seem, then, to promote extrarenal elimination The theory is that the action is due to colloidal changes Excessive changes in the tissue colloids, such as those due to anemia, may explain failures in the treatment of some patients Mejebovskiy expressed the belief that the stasis in the portal system is primary and that the physiochemical changes in the colloids of the endothelium of the vessels and in those of the peritoneum are other factors The chlorine anion plays the funda-

ditions last mentioned, while splenomegaly itself may be a factor, the fact that hemorrhages do not occur frequently in other diseases in which splenomegaly occurs is against such a view. The hemorrhages may be explained as due to obstruction of the venous outflow from the spleen and the intestinal tract as a result of the accompanying hepatic cirrhosis or thrombosis of the splenic vein. Against the theory that infective thrombophlebitis is responsible for the hemorrhages is the absence of abnormalities in the vein at autopsy in most instances.

Abdominal pain and distress, complained of by 50 per cent of the patients in this study, in the cases of severe involvement may be due to occlusion of the mesenteric vessels. Symptoms of intestinal infarction may accompany the pain. In cases of less severe cirrhosis the pain may be due to intermittent claudication of the vessel. A few patients have had several attacks. Perisplenitis is usually responsible for the pain in the upper left quadrant.

According to Hollins ascites alone is a frequent cause of anorexia, vomiting and diarrhea. However, the close relationship of the enlarged spleen and the stomach and the consequent dragging of the spleen on the fundus may be a factor. Splenectomy would, of course, be expected to benefit a patient with such symptoms.

Jaundice and clay-colored stools (observed in 8 cases) are most frequently seen in cases of the obstructive biliary type of cirrhosis. However, at times operation has been performed to relieve the obstruction and the operator has been chagrined to note that the ducts were patent. In such cases the liver is usually atrophic and fibrotic. In this series 86 of 162 patients (53 per cent) had jaundice as determined by the physical findings, history and icteric index. Of the proved cases jaundice was present in 12 but the change in color had not been noticed. Eleven patients who complained of jaundice showed it on physical examination. Fourteen stated that they had been yellow at one time, but no evidence was found at the time of admission. Besides these 37 patients, 8 had neither a history of icterus nor a trace of it on physical examination, but the icteric index was 10 units or above<sup>1</sup>. Of the 78 probable cases jaundice was observed in 18, but it had not been noticed. Seven patients gave a history of jaundice but did not have icterus on physical examination at the hospital. Thirteen complained of being yellow and were found to be so on examination. Three not complaining of jaundice or revealing it on physical examination had an icteric index of 10 or above. Thus, in 45 per cent of the proved cases and in 41 per cent of the probable cases or in 53 per cent of the total number jaundice was present during the course of the disease.

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<sup>1</sup> The normal range is from 4 to 6 units. In clinical icterus the index is above 15. The range for latent jaundice is from 6 to 16 units.

A test of liver function showed fairly marked damage to the liver. The gaseous distention was relieved by the use of salts and enemas, and he left the hospital much improved. One patient is living after thirteen years, but is anemic. Three patients died thirteen years after symptoms began. One of the latter persons was troubled with edema and bloating during the last years of his life. A fourth patient, who had had symptoms for twelve years, died three years after leaving the hospital. He was tapped sixteen times at home. One patient died of hemorrhage in the Minnesota General Hospital eight years after the onset of symptoms. He stated that soon after the symptoms began he was tapped at the Mayo Clinic and was sent home to die, but instead he did hard labor for eight years to within about ten days of his death. One patient is alive and in fair health after seven and one-half years, but he is anemic and jaundiced and complains of swelling of the abdomen and feet. Two others died seven and six years, respectively, after their symptoms began. A woman, six years after the onset of symptoms, is bedridden and edematous and vomits material containing blood. A patient who became ill five years ago is now in fair health except for anemia. One man died three years after the onset of symptoms. Another died two and three-fourths years after symptoms began. He was always jaundiced and had melena at times. He vomited blood the day he died. The diagnosis of cirrhosis was confirmed at autopsy. One patient died after two and a half years of illness. One patient who has lived two years is troubled by abdominal pain and enlargement, and 2 who have lived more than two years complain of weakness. One died at the Mayo Clinic a short time after leaving the Minneapolis General Hospital. He lived two years after the onset. Four others died two years after the first symptoms appeared, 1, fourteen months, 1, six, and 1, five. A patient recently discharged from the hospital is living five months after the onset of illness.

A summary shows, then, that only 9 patients treated medically, and hence classified as probably having cirrhosis, are known to be alive. They are still living nineteen, thirteen, seven and one-half, six, five, two, two and two years and five months, respectively, after the onset of symptoms.

A general study of the records of all the patients who were not treated surgically shows that the duration of life in the group of proved cases was shorter than that in the group of probable cases (table 6). In the former group 100 per cent of the patients died within eleven years, as compared with 67.3 per cent of those in the latter group. At the end of six years the percentages were 93 and 53, respectively. The average for the two groups after six years was 72.6 per cent. In Rowntree's series of patients treated medically, 75 per cent were dead within six years (table 12).

with that of diseases of the heart Autopsy in 7 cases revealed valvular disease, in 1, chronic myocarditis, and in 8, coronary sclerosis

The blood pressure is usually low The average pressure was 118 systolic and 73 diastolic in the proved cases and 123 systolic and 75 diastolic in the probable cases The average pressure for both groups was 120 systolic and 74 diastolic While hypertension was present in a few cases, in more than one-half the blood pressure was below the general average Rest in bed and the general debility associated with the disease are influential factors

TABLE 5—*Laboratory Findings in Cases of Cirrhosis\**

	Proved Cirrhosis	Probable Cirrhosis	Proved and Prob- able Cirrhosis
<b>Blood</b>			
Hemoglobin average percentage	71	72	72
Below 70	32 of 80	20 of 72	52 of 152
Above 90	6 of 80	6 of 72	12 of 152
Erythrocytes average	3,798,000	3,831,000	3,800,000
Below 3,000,000	13 of 71	10 of 64	23 of 135
Above 4,500,000	4 of 71	16 of 64	20 of 135
Leukocytes, average	6,380	6,060	6,220
Below 7,000	32 of 33	33 of 38	65 of 71
Urea nitrogen, mg (average for 38 cases)	25.4	19	23
Wassermann reaction (108 cases)			
Positive	8	10	18
Negative	40	34	82
Positive and negative	3	2	7
<b>Urine (151 cases)</b>			
Albumin	35	36	71
Casts	24	27	51
Sugar	4	6	10
	20 of 26 tested	9 of 15 tested	29 of 41 tested
	11 of 21 tested	16 of 22 tested	27 of 43 tested
	4 of 15 tested	9 of 15 tested	13 of 30 tested
<b>Contents of stomach</b>			
Free hydrochloric acid	11 of 21*	18 of 24†	29 of 45
No free hydrochloric acid	10 of 21	6 of 24	16 of 45
<b>Character of stools</b>			
Clay colored	5	7	12
No bile	4 other cases	1	5
Tarry	4 other cases	3	7
Bloody (red)	2 other cases	3	5
Occult blood	7 other cases	7	14

\* Unless otherwise specified the figures in the columns represent numbers of cases

† The average value for free hydrochloric acid for the group with proved cirrhosis was 19 degrees, for the group with probable cirrhosis, 28 degrees

### LABORATORY FINDINGS

A tendency to anemia and leukopenia is indicated by an average hemoglobin content of 72 per cent and an average erythrocyte count of 3,800,000 (table 5) Readings vary with the technician and the instrument used The table shows the number of hemoglobin readings below 70 or above 90 for each group and also the number of patients with a red cell count below 3,000,000 or above 4,500,000 The average white cell count in all cases was 8,440 In the cases classified as probable instances the average count was 7,450, and in the proved cases, 9,260 When cases of leukocytosis apparently due to inflammation such as pneumonia and peritonitis, were omitted the average count was 6,220,

value is high because of the fairly large percentage of patients who were known to have had the disease for between five and ten years. The course of the disease in these patients, then, was slow, and little credit can be given to surgical intervention for the fact that the patients submitting to operation lived longer on the average than those treated medically.

Of further interest is the finding that the patients lived on the average over a year after the onset of ascites. This value compares favorably with an average period of sixteen months given by Chapman, Snell and Rowntree, from whose paper table 7 is taken. These authors had 28 patients who lived for an average of over thirty-eight months. Forty patients lived or were living longer than the average of sixteen months. Credit for this increase in the length of life after the development of ascites is attributed by the last-mentioned authors in

TABLE 7—*Expectancy of Life After Onset of Ascites as Given by Various Authors\**

Author	Number of Cases	Average Duration of Life After Onset of Ascites, Months
Thacher	7	13
Nissen	26 (paracentesis)	15
	25 (no paracentesis)	10
White	12 (paracentesis)	21
	10 (no paracentesis)	20
Flint	16	50
Ramsbottom	31	60
Chapman et al	112	160
Henrikson	42	128

\* This table was taken in part from the article by Chapman, Snell and Rowntree, 1931.

part to improved methods of treatment. However, that not all the credit should be given to any type of medical management for the apparently better prognosis after the development of ascites is brought out by the finding that of the 42 patients in my series on whom the study was complete and who lived for an average of twelve and eight-tenths months after ascites began, only 2 were given merbaphen, 1 ammonium chloride and mersalyl, 1 aminophylline and 2 magnesium sulfate. The intake of fluids was restricted for 6 patients, and a light diet was ordered for 5. Seventeen patients of the series underwent operation. The question then arises whether the ascites is now recognized earlier both by the patient and by the physician or whether the course of the disease is becoming less progressive. The patients reported on by Chapman, Snell and Rowntree were seen within the last ten years, and those in my series within the last fifteen years. The other authors cited in table 7 reported their findings between 1893 and 1920. Does the Eighteenth Amendment or the section of the country play a part in this difference? Studies of series published elsewhere in the future will help to answer these questions.

The average weight of the spleen obtained at autopsy or by splenectomy in 64 cases was 400 Gm (This does not include a spleen weighing 250 Gm from the 8 year old child or one weighing 150 Gm from the 1 year old child) The average weight of the spleen for normal adults is 150 Gm The largest spleen weighed 1,735 Gm, 41 weighed more than 300 Gm, and 14 weighed 500 Gm or more

The gallbladder was pathologic in 11 instances Eight patients had coronary disease, 7, valvular disease, and 1, chronic myocarditis Esophageal varices were definite in 11 cases In many instances, owing to collapse of the walls, the varices are not observed unless the pathologist distends them by the injection of fluid

### CAUSES OF DEATH

The most common cause of death was hepatic insufficiency, 18 patients dying in coma Some other causes of death were hemorrhage with hematemesis occurring near the time of death in 14 patients, peritonitis in 8, bronchopneumonia in 8 and chronic alcoholism in 5 Six patients died within a day or two after operation Obstructive jaundice and chronic pancreatitis were each present in 4 cases Thrombosis of the portal vein and nephritis were stated as the cause of death in 3 instances each

## TREATMENT OF CIRRHOSIS OF THE LIVER

### MEDICAL MANAGEMENT

Support for the rigid dietary regimen enforced on patients with cirrhosis of the liver appears evident from the experiments of Bollman He has demonstrated the protective value of carbohydrates in instances of cirrhosis of the liver in dogs Cirrhosis was produced by the oral administration of 5 cc of carbon tetra-chloride two or three times a week for about two years More recently, 1 cc of tetra-chlorethane, which is present in a substance used during the World War to waterproof the fabric in airplanes, has been employed The dogs kept on a diet high in carbohydrates (chiefly milk and corn syrup) were little affected by the administration of these toxic substances, while those maintained on a diet of meat frequently showed symptoms of profound toxemia Lesions produced in the liver were less severe in the first group, and the repair was much more rapid Almost perfect repair occurred in several dogs receiving over two hundred doses of carbon tetra-chloride

Ascites was produced experimentally in dogs with obstructive jaundice of several months' duration In the dogs maintained on a diet high in carbohydrates marked ascites developed about twenty-four hours after meat was fed A small amount of meat extract produced



laparotomy In the cases in which ascites is due to portal cirrhosis operation must be performed early, before the liver is too seriously involved He stated that it has long been known that patients with tuberculous peritonitis often recover after simple laparotomy He added that even those with generalized carcinosis survive longer and in comparative comfort when simple drainage under aseptic conditions has been attempted Murrell cited carcinoma as a contraindication, and Wheeler stated that among the patients unsuited for operation are those with ascites due to other causes than cirrhosis of the liver Talma himself listed the following contraindications to operation (1) a high grade disturbance of the function of the liver, (2) icterus, (3) xanthoma and (4) pruritus It was his practice always to tap the patient twice to note the effect before operating White added diabetes, Bright's disease, mental hebetude, pronounced acholia and urobilinuria to the list of contraindications He agreed with Talma that operation is contraindicated if the patient has not withstood several tapplings On the other hand, Allyn stated that repeated tapplings and edema of the feet seem to make no difference in the prognosis but that hebetude, nervousness, restlessness or insomnia is an unfavorable symptom, because it indicates toxemia Most surgeons require that sufficient parenchyma of the liver be present to carry on the hepatic functions Schiassi observed the excretion of urea to gain information on the condition of the hepatic cells O'Malley expressed the belief that operation should be deferred in cases of acute peritonitis and also in instances in which paracentesis shows turbid or heavy ascitic fluid or fluid with a high content of albumin He deferred operation, too, if there was pleural effusion, abdominal pain or elevation of temperature Furthermore, he added glycosuria to albuminuria and urobilinuria as symptoms of poor prognostic import From a study of their own cases Eliot and Colp concluded that as regards prognosis the patients offering the most favorable prognosis are those between the second and the fourth decade of life, who are fairly well nourished, and without severe nephritis, cardiac lesions or signs of collateral circulation, who have withstood a few tapplings, in whom the disease has come on gradually during a year or more, whose liver is of the hypertrophic type and on whom the Schiassi type of omentopexy has been performed with local anesthesia

Rowntree divided cirrhosis into the types in which there is compensation of the liver and those in which there is decompensation He stressed the importance of early diagnosis and treatment If operation is to be performed, it should be before decompensation takes place From a study of 132 cases Greenough found that results were better in patients with an enlarged liver than in those with an atrophic liver, and that the presence of adhesions or perihepatitis was of good prognostic import

mental rôle, and the calcium cation, the secondary rôle. The effect of the calcium chloride is present only when the food is free from salt, otherwise, this medication may favor the accumulation of fluid.

Careful attention must be paid to elimination, both through the urinary tract and by way of the alimentary canal. As regards the use of diuretics, Beckman in his "Treatment in General Practice" stated "It is generally agreed that all the older diuretics nearly always fail to reduce ascites of hepatic origin. Regarding novasurol (merbaphen) it may be said that the majority of the clinicians in Germany, where the drug originated, have been of the opinion that it too was of no avail in these cases" (Brunn, Muhling and Hassencamp were quoted). Bleyer reported good results in 1 case. Fodor maintained that the drug is effective provided the patient has normal blood pressure. In the United States Rowntree, Keith and Barrier stoutly championed its use in connection, it should be noted, with their combination of a low fluid intake, a diet low in salt and the administration of ammonium chloride. They obtained good results in 10 cases, with disappearance of both the ascites and the signs of collateral circulation. The patients improved markedly in health and strength. Chapman stated that jaundice, persistent bleeding from the gastro-intestinal tract and mental disturbances contraindicate the use of diuretics in most instances. Elderly cachectic patients with poor hepatic function may be made definitely worse by their use. In 1930 Rowntree, from an analysis of cases observed during an experience of six years with the use of merbaphen, found that 75 and 85 per cent of the patients in 2 series were benefited by the use of the drug. He stated that the average duration of life after the development of ascites in cases of cirrhosis was found by White and Thompson to be two months, while in his own series of 28 living patients it was 38.4 months. However, 54 per cent of the patients had died within sixteen months, even if the condition was controlled. Eighty-four of the 112 patients who died had lived for an average of fifteen and nine-tenths months. He stressed the importance of early diagnosis and early operation. While the immediate results were good in 80 per cent of the cases in which treatment was medical, 75 per cent of the patients died within six years.

Follow-up letters sent to the patients treated medically at the University of Minnesota and Minneapolis General Hospitals revealed that only a small number could be traced owing to the time elapsed since the patients were hospitalized and to the roving spirit of patients of the type seen in general hospitals. One patient (J. T.) is still living nineteen years after symptoms began. He returned to the hospital after receiving his follow-up letter and was admitted for study because of pain in the right upper quadrant and marked distention of the abdomen.

abdomen above the umbilicus and empty it of fluid. The peritoneum covering the spleen and liver and the parietal peritoneum opposed to them are scrubbed with a dry gauze sponge. The omentum is sutured across the anterior part of the abdominal wall, a glass tube is left in the pouch of Douglas and the parietal wound is closed, silk sutures being used. To keep the parietal and the visceral peritoneum in contact long circular strips of adhesive tape are wrapped about the patient's trunk.

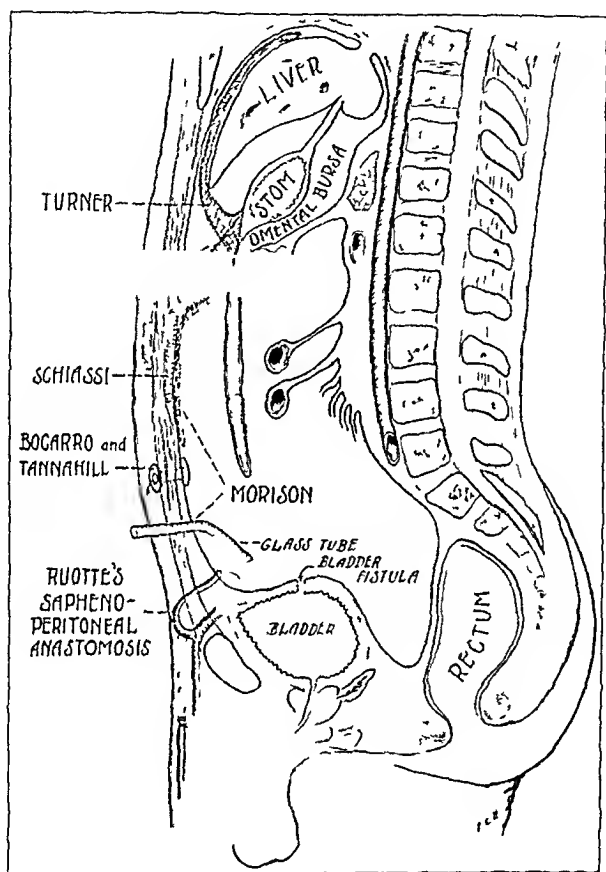


Fig 5—Drawing illustrating the various types of omentopexy and a few other procedures not indicated in figure 4

from the epigastrium to the tube in the hypogastrium. There are many modifications of this operation. Few surgeons use drainage because of the danger of infection, although Morison stated that peritonitis had never developed in his cases. However, Greenough reported a mortality of 50 per cent in 54 cases in which drainage was used, as compared with that of 14 per cent in cases in which no drainage was employed. Turner interposed the omentum between the liver and the

The difference between the group of proved cases and the group of probable cases may be due to the fact that most of the patients with proved cirrhosis entered the hospital in poor condition and died there, while most of those with probable cirrhosis entered and left the hospital in fair condition. Then, too, in the latter group are included those on whom an autopsy was not permitted. Hence, in spite of the typical symptoms and physical findings, these patients may not have had true cirrhosis. The difficulty of diagnosis, even at autopsy, is demonstrated by the necessity of excluding several cases from this study when microscopic examination failed to confirm the diagnosis made from the gross specimen. Studies of series of cases in which the diagnosis of cirrhosis

TABLE 6—*Comparison of Mortality Rates in the Different Groups*

Duration of Symptoms, Years	Unproved Cirrhosis (A) Group in Which Treatment Was Medical (49 Cases), Percentage	(B) Average for Groups A and C (95 Cases), Percentage	Proved Cirrhosis	
			(C) Group in Which Treatment Was Medical (46 Cases), Percentage	(D) Group in Which Treatment Was Surgical (31 Cases), Percentage
1	22.0	41.0	60.0	45.1
2	32.6	48.0	65.2	54.8
3	51.0	62.0	76.0	58.0
4	53.0	67.5	82.5	64.6
5	53.0	69.4	86.9	64.6
6	53.0	72.6	93.0	67.4
7	57.1	75.0	95.6	70.0
8	63.2	78.9	97.8	74.1
9	65.3	81.0	97.8	80.6
10	65.3	81.0	97.8	80.6
11	67.3	81.1	100.0	87.0
12	67.3	83.1		87.0
13	69.3	84.2		
14	73.5	87.0		
15	75.5	87.0		
16	77.5	88.3		
17	77.5	88.3		
18	79.5	89.3		
19	79.5	89.3		
20	79.5	89.3		
21	82.2	90.4		

was based only on symptoms and physical findings cannot be considered trustworthy. Diagnosis based on inspection and palpation of the liver is usually correct, but if the gross specimen is not typically hobnailed, examination of sections under the microscope is essential for positive diagnosis.

Of interest in this summary of the results is the fact that the patients subjected to surgical treatment had lived, even before the operation, over twice as long after the onset of symptoms as had, on the average, the patients not operated on. Patients in the latter group died in an average of eighteen and three-tenths months after the onset of symptoms, while those of the former had had symptoms for an average of thirty-nine months before operation. The average duration of life after operation was five months, thus bringing the total duration of life after the onset of symptoms to an average of forty-four months. This

TABLE 8—Duration of Life After Operation

[illegible]

## SURGICAL INTERVENTION

## PALLIATIVE MEASURES

*Paracentesis*—Mild peritonitis may play a rôle here Cures result from the collateral circulation established by adhesions

## OPERATIVE TREATMENT

*Historical Survey*—The caput medusae perhaps first directed attention to nature's attempt to establish a collateral circulation in cases of cirrhosis of the liver In a postmortem study on persons who had met death by accident Fagge demonstrated that many persons with typical cirrhosis of the liver were in good health, owing to the establishment of a compensatory circulation While he was not the first to show this, his careful and scientific observations were instrumental in placing the subject on a sound basis Talma of Utrecht, Netherlands, in 1887 or 1888, suggested that an attempt should be made to develop a collateral circulation by the establishment of adhesions between the parietal and the visceral peritoneum Van der Meulen attempted to do this for Talma in 1888, but the patient died of shock in a few hours Talma published nothing on the subject until 1898 Lens, of Netherlands, performed a successful operation in 1891, after which the patient lived six months This case was not reported until 1901 A patient of Schley died of peritonitis after operation in 1891 Unaware of the work of these men, Morison, of Newcastle, England, on the suggestion of Drummond, performed an omentopexy in 1894 The patient was not cured but lived eighteen months A short time later another patient was operated on with successful outcome These cases were reported in the first article ever written on the subject in 1896 Other surgeons performing the operation before the close of the century were Howard, 1897, Neuman, of Berlin, 1898, Weir, of New York, 1898, Turner, 1899, and Brown, 1899

*Selection of Patients for Operation*—There is marked diversity of opinion as to what constitutes indications and contraindications for operation on patients with ascites Morison stated that alcoholic cirrhosis is most readily cured and that he has seen no cures in cases of syphilitic cirrhosis Turner agreed that patients with syphilis do badly, while Murrell recommended treating the syphilis medically three weeks and then, if there is no improvement, operating as in other cases Barker reported good results after surgical intervention in such cases White and Thompson advised against operation in cases in which ascites is due to cirrhosis alone, as patients with such a condition hardly ever survive even a tapping for more than a few weeks It is their contention that cure results from operation only in the cases in which there is chronic peritonitis, which in turn is the cause of the ascites Lejars expressed a view that every patient with chronic ascites is benefited by

Paracentesis or continuous external drainage, with rubber or glass drains, is sometimes used

The establishment of a sinus into the bladder has been attempted

4 Splenectomy Gerster and Hartman ligated the splenic artery to produce atrophy of the spleen

An unsuccessful case of splenectomy was reported by Rafferty as early as 1900 Results obtained by Mayo since then would indicate that this procedure is exceedingly helpful in many cases

Splenectomy with a modified Talma procedure seems to be gaining favor

5 Other Procedures According to Rowntree, hemorrhage due to rupture of esophageal varices accounts for a large number of deaths in cases of cirrhosis of the liver He suggested that the collateral circulation be blocked by ligation or injection, so as to preclude the possibility of the portal blood reaching the esophageal varices This was done by Walters in a patient, aged 61, whose stools contained blood daily His procedure was total division of the gastrohepatic omentum, mass ligation of the divided ends and incorporation of the ends into the abdominal incision After operation no blood was present in the stools

Injection of sclerosing solutions into the esophageal varices via the esophagoscope has been considered

Operations, such as cholecystostomy and cholecystenterostomy, are performed in cases in which obstructive symptoms obtain

Diathermy to produce hyperemia has been tried over the liver with benefit

*Results of Surgical Treatment* (tables 8 and 9) —It has been said that statistics concerned with the value of surgical procedures are unreliable, because few men report unfavorable results while most hasten to report favorable results With regard to results in the surgical treatment of ascites this tendency is more than offset by the fact that so many poor results that are published are due to the operation having been performed as a last resort, when little or no benefit could be expected from any treatment Then, too, operations which were devised primarily for the relief of portal cirrhosis are employed in many cases in which the diagnosis is anything but that Authors favoring operation in cases of portal cirrhosis state that this accounts for many poor results, while those opposed to surgical intervention claim that the reported cures occur in cases in which the diagnosis was obscure Cumston cited Willems as admitting only 10 favorable results in 250 cases reported by the Germans Most statistics show improvement in about 50 per cent after operation Of 47 patients operated on at the Mayo Clinic 7 died in the hospital 21 were alive when last heard from,

In the series reported in this paper the results have no definite relationship to the size of the liver or the duration of the ascites. Nor is the duration of the disease of great significance. In one patient the disease may run a rapid course, in another, a slow course. Each patient selected for operation must be studied carefully. Hepatic function, not the size of the liver, the progress of the disease, not the duration, and the condition of the patient in general with special reference to that

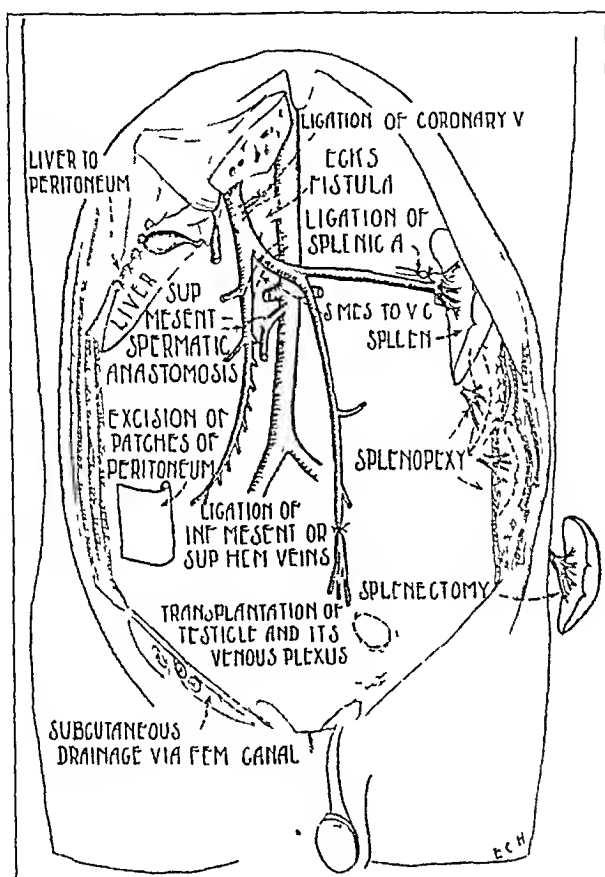


Fig 4—Composite drawing illustrating a few procedures which have been suggested in the surgical treatment of cirrhosis of the liver

of the heart and kidney, not the age or the benefit derived from tapping, are of greatest significance.

In other words, before the patient is subjected to surgical intervention, it must be determined that he is a good surgical risk and that his condition is such that he has a good chance of improving should the operative procedure itself be successfully completed.

*Procedures* (figs 4 and 5)—1 Methods of Establishing Collateral Circulation (A) Omentopexy. Morison's procedure is to open the



2 Of 4 patients on whom a Talma-Morison procedure and a splenectomy<sup>2</sup> were performed, 1 died one hour after operation and 2 on the sixth day after operation, 1 is alive and well three and one-half years after operation

3 Four patients on whom splenectomy<sup>2</sup> only was performed died two, nineteen, one hundred and forty and six hundred and seventy-one days after operation

4 Nine of the 10 patients on whom exploratory operation only was done died in one day, fourteen days, nineteen days, twenty-three days, twenty-seven days, thirty days, six months, four years and four and one-half years after operation, 1 is living eight and one-half months after operation

5 One patient undergoing cholecystogastrostomy lived only one day

TABLE 10—*Duration of Life After Operation*

Type of Operation	Condition of Patient	Less Than 6 Mos	6 Mos to 1 Yr	1 to 2 Yrs	2 to 3 Yrs	3 to 4 Yrs	4 to 5 Yrs	Total Number Patients
Talma Morison	Dead	5	2	1	1			9
	Alive	1 <sup>o</sup>						
Talma Morison and splenectomy	Dead	3						3
	Alive					1 <sup>?</sup>		1
Splenectomy	Dead	3		1				4
Cholecystogastrostomy	Dead	1						1
Cholecystotomy	Dead	1						1
Cholecystoduodenostomy	Dead	1						1
Exploratory operation	Dead	6	1				1	8
	Alive		1				1	2
Ventral herniotomy	Dead	1						1
Summary	Dead	21	3	2	1		1	
	Alive		1			1 <sup>?</sup>	1	
	No trace	1						
		<u>22</u>	<u>4</u>	<u>2</u>	<u>1</u>	<u>1<sup>?</sup></u>	<u>2</u>	<u>31</u>

6 One patient on whom cholecystotomy was performed died three months after operation

7 One patient on whom cholecystoduodenostomy was performed died of peritonitis on the ninth day

8 One patient died two days after ventral herniotomy

A study of this summary and of tables 10 and 11 reveals that in this small series of 31 patients undergoing some type of operation, including exploratory laparotomy and herniotomy, 17 (55 per cent) died within thirty days of the operation. Twenty-one (67.7 per cent)

2 Since these figures were made up, 4 more patients have been operated on at the Minneapolis General Hospital for the relief of cirrhosis. The following results were obtained: C C—Talma-Morison procedure and splenectomy—died two days later, F W—splenectomy—died one day later, G P—Talma-Morison procedure and splenectomy—died one day later, A J—excision of patch of peritoneum followed in one month by splenectomy—died four days later

diaphragm Extraperitoneal fixation of the omentum has become popular Both Schiassi and Barker placed the omentum in a pocket formed between the peritoneum and the posterior surface of the abdominal muscles Narath brought out the omentum beyond the muscle beneath the skin and superficial fascia

(B) Visceropexy Hepatopexy is a possible method Many surgeons as a routine fix the margin of the liver to the peritoneum by a few sutures Others excoriate the surface to encourage the formation of adhesions

Splenopexy was mentioned by Bunge at the Surgical Congress in 1902 By some surgeons the spleen if small is brought out into pockets in the abdominal wall, and if large it is merely sutured to the incision

Lanz, in 1911, transplanted the testicle and spermatic cord to the peritoneal cavity and surrounded them with omentum

Excision of patches of peritoneum has also been recommended as a means of producing collateral circulation through the adhesions thus formed

(C) Ligation of vessels To hasten the formation of the collateral circulation, ligation of the chief tributaries of the portal vein is carried out at times Moynihan ligates the inferior mesenteric vein Mayo ligates the inferior mesenteric or superior rectal vessels as a supplement to epiplopexy

2 Operations in Which a Short Circuit is Effected To relieve the liver of some of the blood entering from the portal system, Vidal made an Eck fistula, after which the patient lived three months

Although often accomplished, anastomosis of the superior mesenteric and spermatic or ovarian veins has not given encouraging results However, Bogoraz and Krestovsky reported good results after anastomosing the superior mesenteric vein and the inferior vena cava

It must be remembered that the liver should not be deprived of too much blood, as such symptoms as convulsions, delirium and coma are said to have resulted when this happened As shown by Pearson, studies on dogs by Hahn, Pawlaw, Massen and Wenckl helped to demonstrate this danger

3 Methods Used for Drainage of Ascitic Fluid Ruotte's saphenoperitoneal anastomosis has given good results in almost 50 per cent of the cases (Griffith) Handley employed the femoral canal for subcutaneous drainage Bocarro and Tannahill reported good results from the use of glass tubes resembling collar buttons which drained into the subcutaneous tissues For the same purpose, other surgeons use silk threads, rubber tubes or sections of blood vessels, but occlusion or obliteration soon takes place

# PROGNOSIS

After careful analysis of the charts the following averages were obtained

Duration of Life	Days	Months
After the onset of symptoms in 75 proved cases in which operations were or were not performed	663	22 1
After ascites developed in 42 cases	385	12 8
With no operation in 45 cases	554	18 3
After the onset of symptoms in 19 cases in which operation for cirrhosis was performed	1,324	44 1
Between the onset of symptoms and operation in 19 cases	1,178	39 2
After operation for cirrhosis in 19 cases	150	5

As has already been mentioned, these values show that the patients subjected to surgical treatment had lived even before operation, more than twice as long after the onset of symptoms as had on the average, the patients on whom no operation was performed. Whether the patients would have lived for an average of five months longer without operation is difficult to state.

TABLE 12—*Comparative Durations of Life After the Onset of Symptoms for Several Series of Patients with Cirrhosis*

	Patients Treated Surgically, Dying Within 6 Years, Percentage	Patients Not Treated Surgically,† Dying Within 6 Years, Percentage
Rowntree's series	66 0	75 0
My series	67 4*	72 5†
Nineteen other series	64 0	

\* This series includes the patients on whom an operation, such as exploratory laparotomy, cholecystotomy, cholecystogastrostomy, etc., was performed, the conditions of most of whom had not been diagnosed as cirrhosis before operation.

† The value 72 5 per cent includes not only the patients treated medically but those who had no medical treatment, owing either to the lack of diagnosis or to the death of the patient soon after admission to the hospital before medical management could be instituted.

In tables 6 and 13 are shown the percentage and number, respectively, of the patients who died during each year after symptoms began. Of the 31 patients undergoing operation, 67 4 per cent died within six years of the onset of symptoms, while 72 5 per cent of those not operated on died within the same period. These statistics correspond closely to those reported by Rowntree (66 and 75 per cent) and to similar values computed on the basis of 108 cases reported in the literature by 19 authors (table 12).

These results are discouraging, to say the least. It is evident that the patient with cirrhosis is a poor surgical risk. With this in mind, the selection of the type of operation must be given serious consideration. Splenectomy or a modified Talma procedure with splenectomy would seem to offer the best possibilities (table 9), but the associated high mortality should make one hesitate to perform these operations on any but those who present the best risks.

Vascular anastomosis, such as Eck's fistula, is far too formidable a procedure for any one to attempt but the surgeon skilled in vascular

Griffith, 1921	Ruotte Dead	5	1	1	1	(14 others)	20%	22%
Birt	Alive							
Bocarro, 1922	Splenectomy						1	1
Gibson and Flick, 1922	Button drain	1						
	Alive and well						1	
	Omentopexy							
	Alive	2	2	1	1	1	2	2
Mayo, 1924	Dead							
	Talma Morison	7						
	Dead	21						
	Alive							
	Splenectomy	7			1	1	1	(17 others)
	Dead	28						
	Alive						4	2
	Splenectomy and Talma Morison	2						(19 others)
	Dead	7						
Jester, 1925	Alive							
	Narath				1			
	Alive							
Tampsky, 1926 (25 cases)	Talma	6						
	Dead	19					1	5
	Alive				1	1	6	13
Hughson, 1927 (26 cases)	Modified Talma, 19, laparotomy, 3, splenectomy, 1, etc	17						
	Dead		7					
	Alive		2					
Tamm III, 1930	I ptiopexy and buttons	1						
	Alive						1	
Bernheim	Ruotte							
	Dead	1						1
Henrikson, 1931 (31 collected cases)	Talma Morison	9						
	Dead	2			1			
	Alive	17						
	Talma Morison and splenectomy	4						
	Dead							
	Alive							
	Splenectomy	4			1			
	Dead							
	Cholecystogastrotomy	2			1			
	Dead	1						
	Cholecystostomy	1						
	Dead							
	Cholecystoduodenostomy	1						
	Dead							
	I xploratory operation	10						
	Dead	6						
	Alive						1	
	Ventral herniotomy	1					1	
	Dead							

surgical technic. Apart from the technical difficulties, this procedure is not recommended for a carnivorous animal like man, because of the danger of flooding the body through the portal circulation with split products from the digestion of proteins.

For patients whose poor condition contraindicates a major procedure one or more of the minor procedures, such as the saphenoperitoneal anastomosis of Ruotte or the establishment of subcutaneous drainage with the use of small glass spools, would seem from reports in the literature to offer hope. Since these procedures aim only at the relief of ascites, however, they appear at best to be palliative. If the patient's condition should improve after the ascites has been controlled, the way would be paved for splenectomy, with or without omentopexy.

An attempt to shut off the venous supply to the lower esophageal vessels to prevent hemorrhage is hardly feasible when the attack is made from below the diaphragm. Bleeding from the many anastomosing branches above the diaphragm would still be a likelihood. Obliterating the lumen of the varices themselves by direct attack through the esophagoscope appears more logical.

#### SUMMARY AND CONCLUSIONS

1 While the etiology of cirrhosis is obscure, the most plausible theory is that portal cirrhosis is caused by toxins or toxin-producing agents brought to the liver by the portal system. (Toxins from the spleen must be considered.) Evidence points to the association of alcohol with the development of cirrhosis.

2 After cardiac and renal pathologic conditions have been ruled out as the underlying process, the clinical diagnosis of cirrhosis of the liver can be made with a fair degree of certainty for a patient, usually a man, in the fourth or fifth decade of life who complains of abdominal pain or distress, nausea and vomiting, constipation or diarrhea, anorexia, hematemesis or melena, associated with general malaise, edema, loss of weight, dyspnea, clinical or latent jaundice and nocturia. On examination he presents ascites, a cardiac murmur, edema, a tendency to jaundice, a palpable spleen, a finely nodular liver (after paracentesis) and often albumin and casts in the urine. The patient usually dies in coma or of hemorrhage or of an infective process.

3 In 84 cases in this series the diagnosis of cirrhosis was proved at autopsy or at operation and by aid of biopsy, and these cases are considered separately. For statistical accuracy only the proved cases should be included in studies of this disease.

4 In the medical or nonsurgical management of cirrhosis judicious selection of cases is essential. The best results were those reported by Chapman, Snell and Rowntree with the use of a special diet, a limited

1 being alive nine years after operation, 1 eight years after, 1 more than seven years after and 1 more than five years after. In an editorial in the *American Journal of Surgery*, June 1909, the following results in 1,565 cases in which omentopexy had been performed were given: (1) patients cured, 30.4 per cent, (2) patients relieved, 19.8 per cent, (3) patients not relieved, 39.2 per cent, and (4) patients dying, 10.6 per cent. In other words, 50.2 per cent were benefited, and 49.8 per cent were not. In a series of 207 cases (included in table 8) selected at random from the reports of 27 authors published since 1909, improvement was noted in 65 per cent and no benefit in 35 per cent. Omentopexy was performed in 108 of these cases, with improvement in 67 and none in 41 (table 9). Splenectomy was performed in 55 cases, with improvement in 45 and none in 10. Saphenoperitoneal anastomosis gave relief in 20 of 42 cases, while in 22 there was no improvement. Button

TABLE 9—Summary of Results of Several Surgical Procedures

	Improvement		No Improvement or Patient Dead	
	Number of Cases	Percentage	Number of Cases	Percentage
Ruotte's saphenoperitoneal anastomosis	20	47.6	22	52.4
Omentopexy	67	62.0	41	38.0
Splenectomy	45	81.8	10	18.2
Button drains	2	100.0		
	134	65.0	73	35.0

drains were used in 2 cases, with improvement in both instances. While the latter series is far from complete, the results in the last half of the period of forty years during which operations have been performed in cases of cirrhosis with ascites indicate an improvement in 65 per cent of the cases in which surgical intervention was used, or in 15 per cent more than in the first half, during which improvement occurred in 50.2 per cent. The most striking results were those of Mayo who obtained improvement in 24 of 28 cases in which omentopexy was performed and in 27 of 34 cases of splenectomy, while the poorest results were those reported by Tempsky, only 7 of 25 patients showing improvement.

The following results were obtained from operations performed on patients in this series:

1. Of 9 patients on whom a Talma-Morison procedure or omentopexy was performed, 8 died in one, eleven, thirty-nine, one hundred and one, one hundred and eighty-three, one hundred and eighty-four, three hundred and sixty-five and five hundred and forty-seven days after operation, 1 left the hospital in good condition after an operation in 1914 and has since been lost track of.

9 In a series of 136 cases reported in the literature, death occurred in 52 per cent within one year of operation. Of my series of 19 patients operated on for cirrhosis, 67 per cent died within one year of operation, while 77.4 per cent of the 31 patients undergoing some type of operation, including such procedures as exploratory laparotomy or herniotomy, died within the same time. Over one-half the patients died within thirty days of operation. These statistics demonstrate the very high mortality rate among patients with cirrhosis.

10 Six years after the onset of symptoms 67.4 per cent of the 31 patients in this series undergoing some form of operation (table 12), 66 per cent of those in Rowntree's series and 64 per cent of those in a series of 108 cases (reported on by nineteen authors) were dead. Compared with values indicated in paragraph 4, these percentages indicate a preference for surgical treatment, were it not for the following facts. In the 19 cases just mentioned the average duration of life from the onset of symptoms to operation was thirty-nine months. The average duration of life after operation was five months, or a total of forty-four months from the onset of symptoms to death, as compared with an average of eighteen and three-tenths months for those whose treatment was medical. The patients undergoing operation had then (even before the operation) lived over twice as long as those without operation. Whether the average length of postoperative life of five months was an increase or a decrease in the expected duration of life is difficult to state.

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died within six months, and 25 (77.4 per cent), within the first year. Operation was apparently a last resort for 5 patients, who underwent surgical treatment ten, ten, eight, eight and seven years, respectively, after the onset of symptoms. These 5 persons lived eleven, two, one hundred and eighty-three, nine and five days, respectively, after operation.

TABLE 11—*Summary of Data on Patients on Whom Operation Was Performed*

No	Age, Yrs	Duration of Symptoms Before Operation	Urea Nitrogen of Blood, Mg	Size of Liver or Weight in Gm	Duration of Ascites	Operation	Duration of Life After Operation
1	67	1 mo		3,180	1 mo	Talma Morison	1 day
2	45	10 yrs		1,560	2 wks	Talma Morison	11 days
3	44	8 yrs	8.9	3,080	2 wks	Talma Morison	6 mos
4	57	9 mos		Palpable		Talma Morison	101 days
5	27	7 yrs		1,400		Talma Morison	5 days
6	23	8 mos	18.6	2,725	6 wks	Talma Morison	183 days
7	51	9 mos		Palpable	9 mos	Talma Morison	39 days
8	40	11 days		Palpable	11 days	Talma Morison	Alive†
9	35	6 yrs	35.0 101.0	1,200	5 yrs	Talma Morison	547 days
10	38	1 yr		Palpable	4 mos	Talma Morison and splenectomy	1 hr
11	57	18 mos	11.2	Palpable	18 mos	Talma Morison and splenectomy	7 days
12	41	5 yrs		Palpable	5 yrs	Talma Morison and splenectomy	3½ yrs *
13	8	2 mos	21.0	525†	2 mos	Talma Morison and splenectomy	6 days
14	42	6 mos		Not palpable	6 mos	Splenectomy	19 days
15	26	10 yrs		2,100		Splenectomy	2 days
16	18	2 wks	11.2	1,450		Splenectomy	11 mos
17	31	6 wks	26.3	950	2 wks	Splenectomy	140 days
18	51	2 yrs	14.0	Palpable		Cholecystotomy	3 mos
19	34	6 wks		Palpable		Cholecystogastrostomy	1 day
20	46	8 yrs	19.6	2,360		Cholecystoduodenostomy	9 days
21	50	9 mos	2.4	2,370		Ventral herniotomy	2 days
22	45	5 days	42.0	Not palpable		Exploratory	1 day
23	31	1 mo		3,140		Exploratory	4½ yrs
24	63	1 yr		Palpable		Exploratory	19 days
25	57	2 mos		Palpable	1 mo	Exploratory	23 days
26	48	4 mos		Palpable		Exploratory	4 yrs *
27	49	3 wks	9.1	Palpable		Exploratory	2 wks
28	18	4 mos	15.0	Palpable		Exploratory	8½ mos *
29	47	8 wks	23.3	Palpable	9 days	Exploratory	1 mo
30	13	6 mos	16.8	1,110†	4 mos	Exploratory	6 mos
31	26	1 mo		Not palpable	1 mo	Exploratory	8 days

\* Patient alive

† Patient lost track of after leaving the hospital

‡ Child

One patient who had an exploratory operation four months after the symptoms began is alive and well four years after operation. Another operated on five years after the development of ascites is alive and well three and one-half years after omentopexy and splenectomy. A third patient is still living eight and one-half months after operation, and a fourth was lost track of after the operation.

Eight patients who were 50 or past lived one hundred and one, ninety, thirty-nine, twenty-three, nineteen, seven and two days and one day after operation. In general, the older patients did not do well



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TABLE 13—Duration of Life After the Onset of Symptoms

[illegible]

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intake of fluids, ammonium nitrate or ammonium chloride, merbaphen or mersalyl and at times the employment of purines as diuretics. Only carefully selected patients were treated. The average length of life after the onset of ascites for the patients in their series was sixteen months, while in 28 cases it was thirty-eight months, as compared with an average of twelve and eight-tenths months in the series reported in this paper, in which there was no special management. At the end of six years 75 per cent of the patients reported on by the aforementioned authors were dead, as compared with 72.6 per cent of the patients without surgical treatment in this series. The values were 93 and 53 per cent, respectively, for the two groups, of proved and probable cases (table 6).

5 In the selection of patients for operation a careful study of the liver, kidneys and heart should be made to determine (a) whether the patient is a good surgical risk and (b) whether he has a good chance of improving later should the operative procedure itself be successfully completed. Early diagnosis and early operation should improve the results.

6 The type of operation should depend on the condition of the patient. If he is a poor surgical risk, paracentesis may be the only procedure indicated. Other procedures for controlling the ascites, such as the use of collar-button-like tubes draining into the subcutaneous tissues and the saphenoperitoneal anastomosis of Ruotte, are reported as giving good results. The more formidable procedures attempting (a) to establish collateral circulation and (b) to decrease the volume of blood storming the harassed liver via the portal gate, such as the establishment of an Eck fistula, anastomosis of the superior mesenteric vein and the inferior vena cava, splenectomy, the Talma-Morison procedure or one of its modifications or a combination of omentopexy and splenectomy, are indicated only in especially selected, well prepared patients because of the associated high mortality rate.

7 The multiplicity of operative procedures devised for the relief of patients with cirrhosis indicates their inadequacy. The failure of some types to give relief can be explained by (a) the technical difficulties involved in carrying out the procedure, (b) the mechanical failure of the procedures even when properly performed and (c) their use as a last resort in patients who are poor risks, with the consequent high rate of mortality.

8 The results of surgical treatment reported in the literature vary widely, the most striking being those reported by Mayo, which indicated improvement in 24 of 28 cases in which omentopexy was performed and in 27 of 34 cases in which splenectomy was performed. The poorest results are those reported by Tempsky which indicated improvement in only 7 to 25 cases. In a series of 250 cases Cumston cited Willems as admitting favorable results in only 10 cases.

# EFFECT OF REMOVAL OF STELLATE SYMPATHETIC GANGLION ON GROSS AND HISTOLOGIC STRUC- TURE OF THE THYROID GLAND

AN EXPERIMENTAL STUDY

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Since Koeben<sup>1</sup> in 1855 first suggested the sympathetic origin of disease of the thyroid, numerous investigators have attempted to prove or to disprove his theory

It has been demonstrated by Anderson,<sup>2</sup> Berkley<sup>3</sup> and Rhinehart<sup>4</sup> that the thyroid is amply supplied by nonmedullated nerves, ending in fine fibrils, with knoblike enlargements on the basal ends of the gland cells Briau<sup>5</sup> has shown by anatomic and embryologic dissections that the thyroid nerves come from the cervical portion of the sympathetic trunk, arising in the main from the middle of the cervical portion of the trunk in man and from the inferior cervical or stellate ganglion in the dog and cat It has also been demonstrated that ganglion cells exist both in the superior laryngeal nerves<sup>6</sup> and in the thyroid gland<sup>7</sup>

In the attempt to demonstrate a functional relation between the thyroid and its nerve supply many conflicting reports of experimental studies have been made These include various histologic changes after

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thyroid gland or stellate ganglion was removed through a midline incision. In all the dogs the wounds healed per primum, and at the termination of the experiments specimens were first removed with the animals under anesthesia, and then the animals were killed. Specimens were immediately placed in solution of formaldehyde and Zenker's fixative and then stained with Weigert's hematoxylin and eosin.

TABLE 1—*Comparison of Lobes of the Thyroid Gland of Dogs After Unilateral (Right) Lobectomy*

Dog	Time Between Operation and Death	Breed of Animal and Age	Hyperplasia		Round Cell Infiltration		Vascularity		Colloid		Comment
			L	R	L	R	L	R	L	R	
301	8 mo	Fox terrier, 6 to 7 yr	+	++	+	+	+	++	+	+++	
317	18 days	Beagle 10 mo	+	++	+	+	+	+	++	++	
320	7 mo 1 day	Poodle, 2 yr	+	+	++	++	+	+	++++	++++	No striking differences between lobes
325	7 mo 8 days	Fox terrier, 2 yr	+	++	+	+	+	+	++	+++	
334	3 mo 23 days	Mongrel 3 yr	++	+	+	+	+	+	+	++	

TABLE 2—*Comparison of Lobes of the Thyroid Gland in Dogs After Unilateral and Bilateral Stellate Ganglionectomy*

Dog	Time Between Operation and Death	Breed of Animal and Age	Hyperplasia		Round Cell Infiltration		Vascularity		Colloid		Comment
			L	R	L	R	L	R	L	R	
304	7 mo 23 days	Mongrel 2 to 3 yr	+	+	+	+	+	+	+	+	Ganglionectomy on left; died of dysentery postmortem changes in thyroid but no apparent difference
307	8 mo 2 days	Mongrel, 6 mo	+	+	+	+	+	+	++	++	Ganglionectomy on left
256	3 mo 21 days	Mongrel 1 to 2 yr	+	+	+	+	+	+	+++	++	Bilateral ganglionectomy
321	7 mo	Mongrel 1 yr	+++	+	+	+	+	+	+	+	Ganglionectomy on left
Puppy 1	23 days	Collie 4 wk	+++	+++	+	+	+	+	+	+	Ganglionectomy on left
Puppy 2	26 days	4 wk	++	++	+	+	+	+	+++	+	Bilateral ganglionectomy

#### UNILATERAL LOBECTOMY OF THE THYROID

Several experiments were carried out to study the effect of unilateral lobectomy on the normal thyroid under conditions prevailing during this study. It was noted that the two lobes of the thyroid in the same animal were similar but that thyroids removed from different animals showed considerable variations (table 1). This was corroborated by the

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2 No definite changes could be demonstrated in the remaining lobe of the thyroid, using one lobe as a control, after (a) unilateral lobectomy, (b) cervical ganglionectomy and (c) unilateral lobectomy and simultaneous ganglionectomy on the opposite side

#### PROTOCOLS

All operations were performed under sterile technic through a midline incision in the neck extending from the manubrium to the thyroid cartilage. Black silk sutures were used throughout.

The specimens were fixed in a solution of formaldehyde and Zenker's solution.

Dog 301—A white male fox-terrier 6 or 7 years old underwent an operation for removal of the right lobe of the thyroid on Sept 29, 1931. The dog remained healthy, with no apparent change in its habits or reactions. It was killed on June 1, 1932, at which time the left lobe of the thyroid was removed for comparison.

Dog 317—A female beagle puppy about 10 months old underwent an operation for removal of the right lobe of the thyroid on Oct 9, 1931. Recovery was uneventful, and the dog was in good health until October 24, when it contracted distemper. It died on Oct 26, 1932. Autopsy revealed pneumonic consolidation of both lungs. The operative field was in good condition. The left lobe of the thyroid was removed for comparison.

Dog 320—A female police dog about 2 years old underwent an operation for removal of the right lobe of the thyroid on Oct 16, 1931. The left lobe was inspected. The dog remained well and healthy, with no change in its habits or reactions until it was killed on May 17, 1932, at which time the left lobe was removed. The operative field was in good condition. There was no apparent change in the size of the left lobe.

Dog 325—A female fox-terrier about 2 years old underwent an operation for removal of the right lobe of the thyroid on Oct 20, 1931. The left lobe was inspected. The dog remained healthy and in good condition with no change in its habits. It was killed on June 16, 1932, at which time the left lobe of the thyroid was removed. There was no apparent change in its size.

Dog 334—A mongrel collie, a male, about 3 years old, underwent an operation for removal of the right lobe of the thyroid on Dec 23, 1931, and the left lobe was inspected. The dog remained in good health with no change in its habits. It was killed in a fight on March 26, 1932. The left lobe of the thyroid was removed. There was no apparent change in its size.

Dog 303—A brown female about 1 year old underwent an operation for removal of the right lobe of the thyroid and the left stellate ganglion on Sept 30, 1931. Immediately following the operation the left pupil was contracted, both pupils reacted to light. Postoperatively the left pupil was contracted to one-half the size of the right pupil. Both reacted to light. Enophthalmos and lid lag were present in the left eye, and the conjunctiva was redundant over the sclera.

Three weeks postoperatively both eyes were the same, except for the pupillary difference. The right pupil was twice the size of the left. One month after the operation the dog had repeated convulsions. It was killed on October 30. Autopsy revealed pneumonia almost filling the entire right side. The operative site was in good condition. The left lobe of the thyroid was removed for study.

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Dog 305—A black and tan female about 2 years old underwent an operation for removal of the right lobe of the thyroid and the left stellate ganglion on Oct 5, 1931. Immediately following the operation the left pupil was one-half the size of the right pupil. Both pupils reacted to light. The dog remained in good health, with no apparent change in habits. During the next seven months of observation the left pupil was constantly smaller than the right, slight enophthalmos, lid lag and redundancy of the conjunctiva persisted. Infection developed in a dog-bite wound in the thoracic wall on the left side, and the dog was killed on May 12, 1932. The left lobe of the thyroid was removed. There was no apparent difference in the size of the lobes.

Dog 318—A large brown male from 4 to 5 years old underwent an operation for removal of the right lobe of the thyroid and the left stellate ganglion on Oct 3, 1931. The usual changes were observed. The left pupil was one-half the size of the right. Both reacted to light. Enophthalmos, lid lag and redundancy of the conjunctiva were present in the left eye. Lid lag and enophthalmos disappeared after four months. The animal remained healthy, with normal habits. It was killed on May 21, 1932. The left lobe of the thyroid was removed. There was no apparent change in size.

Dog 326—A brown mongrel female about 8 months old underwent an operation for removal of the right lobe of the thyroid and the left stellate ganglion on Nov 2, 1931. The usual changes occurred in the eyes. Four days after the operation the dog contracted distemper, and it died twenty-eight days postoperatively. The left lobe of the thyroid was removed.

Dog 336—A mongrel male 1 year old underwent an operation for removal of the right lobe of the thyroid and the left stellate ganglion on Dec 15, 1931. The usual changes occurred in the eyes. One month after the operation the dog contracted distemper, and it died on Jan 30, 1932. The left lobe of the thyroid was removed.

Dog 358—A black and white female about 1½ years old underwent an operation for removal of the right lobe of the thyroid and the left stellate ganglion on Feb 15, 1932. The usual changes occurred in the eyes. The left pupil was one-half the size of the right. The conjunctiva was redundant. Enophthalmos and lid lag were not apparent. The dog remained healthy, with normal habits, until it was killed on June 6. The left lobe of the thyroid was removed.

Dog 304—A brown and white male mongrel 2 or 3 years old underwent an operation for removal of the left stellate ganglion on Oct 2, 1931. The usual changes occurred in the left eye: small pupil, enophthalmos, lid lag and redundant conjunctiva over the sclera. Enophthalmos and lid lag disappeared four months after the operation. The dog remained healthy, with normal habits. It was killed on May 25, 1932. The right and left lobes of the thyroid were removed.

Dog 307—A black and tan female about 6 months old underwent an operation for removal of the left stellate ganglion on Oct 6, 1931. The usual changes occurred in the eyes and persisted until death, although enophthalmos, lid lag and redundancy of the conjunctiva gradually receded. The dog remained in good health and of normal habits. It was killed on June 8, 1932. The right and left lobes of the thyroid were removed.

Dog 321—A brown female mongrel about 1 year old underwent an operation for removal of the left stellate ganglion on Oct 20, 1931. The usual changes occurred in the left eye. The dog remained healthy, with normal habits. Corneal

the administration of pilocarpine,<sup>8</sup> not confirmed by others,<sup>9</sup> both degeneration<sup>10</sup> and hyperactive changes<sup>11</sup> following stimulation of the sympathetic nerves (likewise contradicted by other findings<sup>12</sup>), histologic changes after division of the cervical sympathetic chain<sup>13</sup> and after division of the laryngeal nerves,<sup>14</sup> absence of histologic changes after bilateral removal of the laryngeal nerve,<sup>15</sup> and similarity of transplanted and intact thyroid glands<sup>16</sup>

Great variations in the physiology of the gland, estimated by various procedures, have been reported. The thyroglobulin content of the thyroid has been observed to be increased following the injection of epinephrine<sup>17</sup>. The iodine content has been observed to be decreased<sup>18</sup> and unchanged<sup>19</sup> following the stimulation of the sympathetic trunk while another investigator reported a decrease after the division of the cervical portion of the sympathetic trunk.<sup>13b</sup>

The conclusions cited previously regarding the histologic change in the thyroid after division of its sympathetic supply were based in some instances on observations on one or two animals. For that reason the problem was again undertaken, twenty dogs being used, all of which were studied under identical conditions. The operations were performed with strictly aseptic technic. Ether was used as the anesthetic, the neck was shaved and cleaned with iodine and alcohol and a lobe of the

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19 Van Dyke H. *Am J Physiol* **56** 168, 1921.

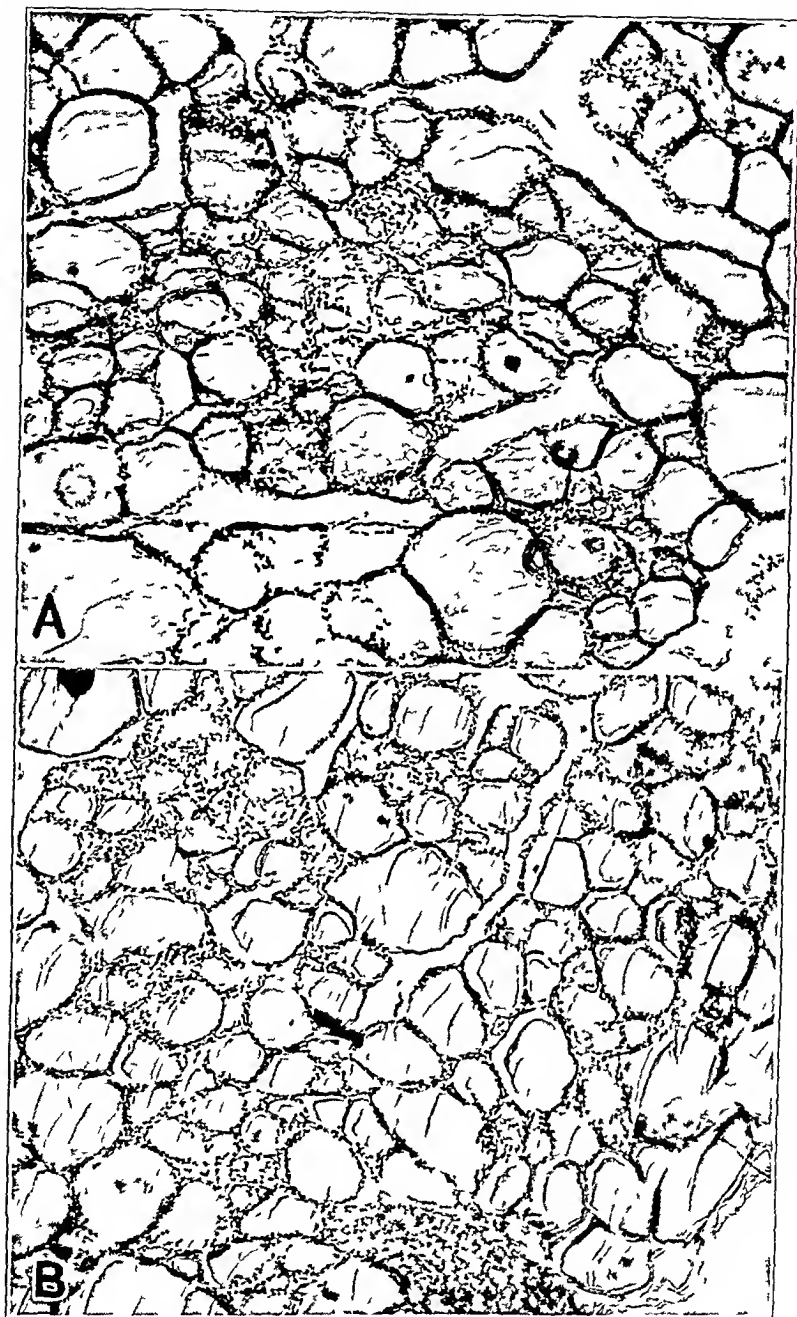


Fig 3 (dog 326) —The effect of removal of the left stellate ganglion and the right lobe of the thyroid. The photomicrographs show *A*, a section of the right lobe, and *B*, a section of the left lobe taken one month and one day after the operation. There is no appreciable difference between the microscopic sections.

studies of several investigators<sup>20</sup> The fact that great differences exist between normal thyroids cannot be too strongly emphasized when one makes an appraisal of the results of an experiment of this kind

# UNILATERAL AND BILATERAL STELLATE GANGLIONECTOMY

In this series the left stellate ganglion was removed except in two animals, in which both ganglions were removed The thyroid was not disturbed Only animals exhibiting postoperative pupillary changes enophthalmos and redundant conjunctiva were included in this series Further proof that the cervical chain was removed was gained by microscopic examination After varying periods of time we could find no definite changes in the thyroid glands which might serve to distinguish them from the lobes of thyroids removed in the first series (table 2)

TABLE 3—Comparison of Lobes of the Thyroid Gland of Dogs After Removal of the Right Lobe and the Left Stellate Ganglion

Dog	Time Between Operation and Death	Animal and Age	Hyperplasia		Round Cell Infiltration		Vascularity		Colloid	
			L	R	L	R	L	R	I	R
70	1 mo	Brown 1 yr	—	—	—	—	—	—	—	—
705	7 mo 1 day	Black and tan 2 yr	+	—	+	—	—	—	—	—
715	7 mo 1 day	Large brown 4 to 5 yr	—	—	—	—	—	—	—	—
20	1 mo 1 day	Brown mongrel 9 mo	+	—	—	—	—	—	—	—
750	16 days	Mongrel 1 yr	—	—	—	+	—	—	—	—
758	7 mo 2 days	Mongrel, 2 yr	—	—	—	—	—	—	—	—

# UNILATERAL LOBECTOMY AND GANGLIONECTOMY OF THE OPPOSITE SIDE

In this series the right lobe of the thyroid and the left stellate ganglion were removed at the same time Again no changes could be seen in the remaining lobe of the thyroid which could honestly be said to distinguish it from the normal lobe (table 3)

# CONCLUSIONS

1 The fact that in the normal dog there are wide variations in the histologic appearance of the thyroid gland is important in the appraisal of the results of an experiment of the kind described

<sup>20</sup> Fuhr F Arch Exper Path u Pharmacol 21 387 1886 Halsted W S Tr A Am Physicians 28 127 1913 Hunnicutt I A Am J M Sc 148 207 1914 Watts C Wiener 15b Rile, Rogers and Fawcett 15

# OSTEOMYELITIS OF INFANTS

A DISEASE DIFFERENT FROM OSTEOMYELITIS OF OLDER CHILDREN

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Osteomyelitis of infants (children under 2 years of age), if one may judge from the literature, has usually been considered a rare disease not essentially different from the osteomyelitis of older children. This has been so contrary to our experience that we have reviewed the cases of patients of this age group treated at the Children's Hospital of Boston during the last twenty-one years—in all, 95 cases. In this survey we not only have considered the acute phases of the disease but have determined by recent clinical and roentgenographic examinations the present status of 41 patients treated in the orthopedic service during the aforementioned period. In some instances this observation was made as long as twenty years after the original infection.

We have included cases of both acute and chronic osteomyelitis in this study, although primary consideration has been given to the acute disease. On the basis of classifying a condition with a duration of one month or longer at the time of the patient's admission to the hospital as chronic, the condition in 82 of the 95 cases was acute and in 13 chronic osteomyelitis. In only 4 of the cases of so-called chronic osteomyelitis was the duration longer than three months, many cases were instances of healing acute osteomyelitis.

For general statistical information we have used the data on all the cases, but in the consideration of treatment we have used only those on cases of acute osteomyelitis, as it is only in those cases that the treatment was followed throughout the course of the disease.

In the entire series the mortality rate was 21 per cent. Separate consideration of the cases of infants under 6 months of age reveals a mortality rate definitely higher, 45 per cent, whereas in infants over 6 months and under 2 years of age the mortality rate was 14 per cent.

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Read in part before the Boston Orthopedic Club, March 1933

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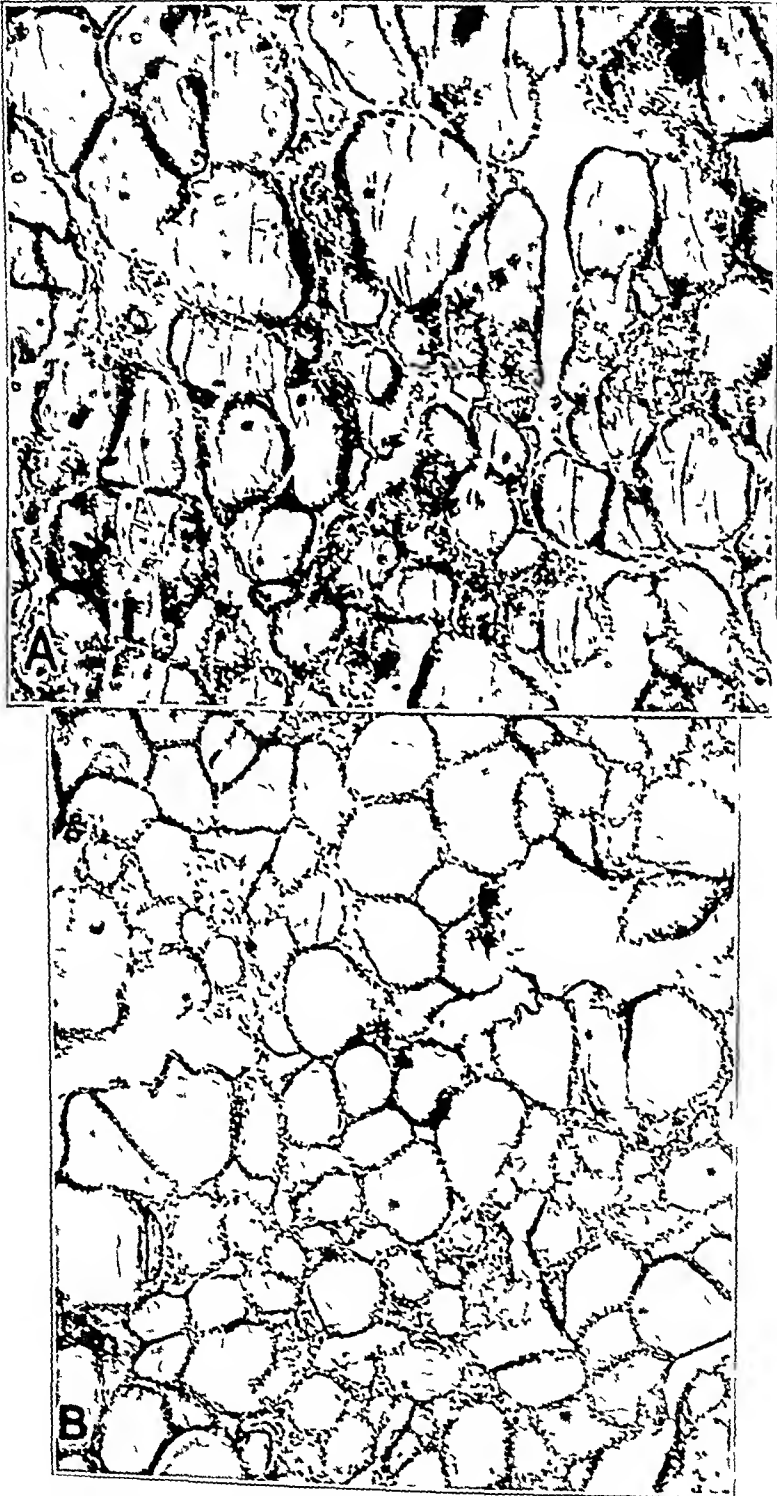


Fig 1 (dog 320) —The effect of unilateral thyroidectomy on the remaining lobe. The photomicrographs show *A* a section of the right lobe, and *B* a section of the left lobe taken seven months and one day after the removal of the right lobe. There are no striking differences.



## PREDISPOSING FACTORS

*Antecedent Infection*—The relationship of antecedent extra-osseous infection in this group is striking, in that 52 patients (table 1), or approximately 55 per cent, had undoubted preceding infections, as shown either by a definite history or by physical findings at the time of admission to the hospital (We have not included such doubtful evidence as chronic tonsillitis and other questionable findings) In 43 cases the evidence of infection either was doubtful or was omitted from the history It is possible that in many instances the person recording the history neglected to inquire as to the presence of recent infection

As may be seen in table 1, infection of the respiratory tract was present in 28 patients, or in approximately one half of the 52 in whom antecedent infection was known to be present Of these, 20 had colds, bronchitis or sore throat 3 had pneumonia with or without empyema, 2 had otitis media and 3 had infection of the respiratory tract with

TABLE 1—*Relation of Extra-Osseous Infection and Trauma to Osteomyelitis*

	Cases		Cases
Incidence of antecedent infection	52	Incidence of trauma	16
Infection of respiratory tract	28	With antecedent infection	6
Cutaneous lesions	13	Without antecedent infection	10
Omphalitis	4		
Miscellaneous infections	7		
No known antecedent infections	43	No history of trauma	79

other abscesses Antecedent infection of the respiratory tract occurred in 30 per cent of the total number of cases

Antecedent cutaneous lesions were present in 13 cases, which was one fourth of those in which there was known to be an antecedent infection, or approximately 14 per cent of the entire group The lesions were, specifically furuncles, 4 cases, infected wounds, including burns, 4, impetigo, 2, paronychia, 1, scabies, 1, and eczema, 1

Omphalitis was present in 4 cases, in each of which the patient was in the first weeks of life Miscellaneous infections included measles, 3 cases, chickenpox, 2, gonococcic septicemia (maternal origin), 1, and congenital syphilis, 1

We should note that 5 patients had acute rickets and 2 were mongolian idiots, whose resistance to infection is notoriously poor

*Trauma*—The relationship of injury to osteomyelitis has been frequently debated Ullmann, Lexer<sup>3</sup> and others<sup>4</sup> demonstrated that

3 Lexer, Erich Zur experimentellen Erzeugung osteomyelitischer Herde, Arch f klin Chir 48 181, 1894, Experimente über Osteomyelitis, ibid 53 266, 1896, Osteomyelitis Experimente, ibid 52 576, 1896, General Surgery, translated by A D Bevan, New York, D Appleton & Company, 1910

4 Robertson, D E Acute Hematogenous Osteomyelitis, J Bone & Joint Surg 25 8, 1927

ulceration and cataract developed in the left eye. It was killed on May 20, 1932. Both lobes of the thyroid were removed.

Dog 356—A brown female about 1½ years old underwent an operation for removal of both stellate ganglions on Feb. 15, 1932. Both eyes showed immediate



Fig. 2 (dog 307)—The effect of unilateral ganglionectomy on the thyroid gland. The photomicrographs show A, a section of the left lobe, and B, a section of the right lobe. In spite of removal of the left stellate ganglion eight months and two days previously, there are no striking differences between the microscopic sections of the two lobes.

changes, i. e., contracted pupils, enophthalmos, redundant conjunctiva and slight lid lag. The enophthalmos and lid lag gradually decreased but persisted until death. The dog received 15 grains (0.975 Gm.) of thyroid extract three times a day at

coccus was obtained there were 7 deaths, a mortality rate of 32 per cent. The higher rate in cases of staphylococcic infection is further emphasized when one considers only cases of acute osteomyelitis, in which the mortality rate from streptococcic infection was 19 per cent and that from staphylococcic infection was 41 per cent. Considering all cases in infants under 2 years, one sees that staphylococcic osteomyelitis definitely caused a higher mortality rate than streptococcic osteomyelitis.

In a separate consideration of the cases of infants under 6 months of age, one obtains a different picture. Of the 23 infants under 6 months of age, 10 had a streptococcic infection and 6 of these died, a mortality rate of 60 per cent, 5 had a staphylococcic infection and 2 of these died, a mortality rate of 40 per cent (table 2). This suggests that

TABLE 2—*Bacteriologic Incidence, Showing a Relation of the Organism and Age to Mortality*

Organism	All Patients			Patients Under 6 Mo of Age			Patients from 6 Mo to 2 Yr of Age		
	Patients	Deaths	Mortality per Cent	Patients	Deaths	Mortality per Cent	Patients	Deaths	Mortality per Cent
Streptococcus	48	10	20	10	6	60	35	4	10
Staphylococcus	22	7	32	5	2	40	17	5	30
Pneumococcus	3	1		0	0		3	1	
Gonococcus	1	0		0	0		2	0	
Undifferentiated coccus	2	0		1	0		0	0	
Cases in which culture was recorded	76								
Cases in which culture was not recorded	19	2		6	2		13	0	
Total	95	20	21	22	10	45	73	10	14

streptococcic osteomyelitis is relatively more virulent in infants under 6 months of age than in older infants.

*Chronic Osteomyelitis*—Of the 13 cases of chronic osteomyelitis, there were 8 in which a culture was made. In 5 *Staph aureus* was present, in 2, *Strep haemolyticus*, and in 1, *Pneumococcus*.

When one considers the relative infrequency with which *Staphylococcus* is isolated in cases of acute osteomyelitis of infants (25 per cent), the presence of this organism in 5 of the 8 cases of chronic osteomyelitis would seem to have some significance, although there are too few cases for one to draw any conclusions. *Staph aureus* seems to produce chronic osteomyelitis more frequently than *Str haemolyticus*, even in infants.

*Blood Culture*—Cultures of the blood were not made as a routine procedure and usually were made only when the patient was severely ill. Of the cultures of the blood recorded for 24 cases, 10 yielded *Streptococcus*, 6 *Staph aureus* and 1 *Staph albus-haemolyticus*, and 7

various intervals, with coincident increase in the pulse rate and loss of appetite but no changes in the eyes. The dog was killed on June 2. The right and left lobes of the thyroid were removed.

PUPPY 1—A small brown collie 6 weeks old underwent an operation for removal of the left stellate ganglion on Oct. 3, 1931. There were the usual changes on the left. The puppy progressed well for the first two weeks post-operatively and then rather suddenly went down-hill and died, probably of distemper, on October 29. At autopsy both lobes of the thyroid were removed. Intestinal worms were present.

PUPPY 2—A small brown puppy 7 weeks old underwent removal of both stellate ganglions on Oct. 8, 1931. The eyes showed characteristic changes bilaterally. The puppy did well for three weeks and then gradually grew feeble and died. Autopsy revealed an abscess in the abdominal wall, probably secondary to an infected bite. The right and left lobes of the thyroid were removed.

infection of the soft tissue, scurvy, with infection elsewhere, and syphilis are less confusing. Rheumatic fever is not a consideration at this age.

Sepsis of a joint frequently causes diffuse swelling surrounding the joint, though usually the swelling is not as widespread as in cases of osteomyelitis. The presence of a resistant flexion deformity, marked muscle spasm and pain on motion, associated with synovial tenderness and distention of the capsule, suggests sepsis of the joint. Occasionally a joint may show considerable distention with fluid provoked by adjacent osteomyelitis without the joint's being infected, but the amount of fluid in a joint so involved is less than one would expect from the severity and duration of the infection, and motion is less painful. Aspiration of the joint through clean tissue may be necessary before the diagnosis can be made, and even then it may be necessary to await culture of the fluid. Sepsis of a joint secondary to adjacent osteomyelitis is always a possibility, as in infants secondary sepsis of the joints is more common than in older patients.

Ordinarily superficial cellulitis is easily differentiated, but cellulitis or abscess of the deeper fascial layer and suppurative bursitis may be very perplexing, and often preoperative differentiation cannot be made. If involvement of the part is most marked at a distance from the epiphysis, it is suggestive of a process in the soft tissues. Osteomyelitis in children almost uniformly has its origin adjacent to the epiphysis.

The multiplicity of the lesions, the general picture and the laboratory observations serve to differentiate syphilis. As far as scurvy is concerned, the prime consideration is to keep it in mind in arriving at the diagnosis.

*Roentgenography*—Roentgen examination is of more diagnostic aid for infants than for older children or adults, since the lesions are visible at a somewhat earlier period in the disease. The distribution of edema in the soft tissue as visible in the roentgenograms is occasionally helpful. Likewise, the roentgenograms may be of aid in the differential diagnosis by demonstrating the distended capsule of a septic joint or by suggesting the presence of scurvy or syphilis.

In addition to early juxta-epiphyseal rarefaction, one should look for the formation of subperiosteal new bone, which occasionally is the first abnormality that can be observed.

Roentgenographic observations of the course of the disease are illuminating. The subperiosteal new bone (involucrum) is visible much sooner than in older persons, it usually involves half the length of the bone and frequently suggests that sequestration of the shaft will occur, but, as will be seen later, this rarely happens. The healing process as visible in the roentgenograms likewise occurs much more rapidly than in older persons.

## AGE AND SEX

Osteomyelitis is reported as being most common between the ages of 8 and 16 years. For example, Wade<sup>1</sup> of the Royal Alexandra Hospital for Children in Sydney, Australia, reported on 613 cases, in which the highest incidence was in children between 9 and 11 years. He stated that in his series there were few patients under 3 months of age and practically none between that age and 2 years.

On the basis of our experience osteomyelitis in the younger group of children is not rare. This was particularly emphasized by the fact that in the Children's Hospital (age limit 12 years) during the last two years there were more patients under 2 years of age than over 2 years, namely, 35. We do not believe that this represents a true relative age incidence, but it does suggest that osteomyelitis in this group is not unusual.

The patients in this series were evenly distributed through the various age groups under 2 years, 23 were under 6 months, the youngest being 11 days.

There were 50 boys and 45 girls. Osteomyelitis is more frequent in males than in females, and this has been ascribed to their greater exposure to trauma. On this basis one would not expect any particular difference in this series, and there was very little.

## BONES INVOLVED

Klemm<sup>2</sup> reported that in 385 lesions the femur and tibia were almost equally involved, the femur in 111 instances and the tibia in 101. In our series 121 bones were involved in 95 cases. The femur was involved in 48 cases, the tibia in 18, the humerus in 16 and other bones less frequently. Multiple lesions were present in 12 cases, in 3 there being 4 or more. The femur was by all odds the bone most frequently involved.

The more rapidly growing end of the bone was involved in most cases. For example, in only 12 of the 48 cases of involvement of the femur was the lesion in the upper end, in 7 the neck was involved, and in 3, the greater trochanter. Likewise, in all of 9 cases in which the radius, with the preponderance of growth at the lower end, was involved, the lesion occurred in the lower end. In the tibia, where growth is little more rapid at the upper than at the lower end, the upper end was involved in 11 cases and the lower end in 7 cases.

<sup>1</sup> Wade, R. B. *Acute Osteomyelitis of Children*, M. J. Australia **1** 264, 1929.

<sup>2</sup> Klemm, P. *Beiträge zur Kenntnis der infektiösen Osteomyelitis*, Beitr. z. klin. Chir. **84** 352, 1913.

In considering the foregoing factors alone, one conceives that the course of osteomyelitis in infants is quite different from that in older children. In infants there is a pleasing contrast from the frequently prolonged disease with long periods of hospitalization and repeated surgical procedures that are commonly observed in older children.

*Complications*—The most common complications were lesions of other bones, sepsis of joints, pneumonia and abscesses, both fascial and visceral. Twelve patients had lesions of more than one bone. Sepsis of joints occurred in 11, in 9 by apparent extension from an adjacent bone, and in 2 as a metastatic lesion without evident involvement of adjacent bone. Of the first mentioned group, 4 had involvement of the hip joint from adjacent osteomyelitis of the neck of the femur, 3 involvement of the knee joint from the femur and 2 involvement of

TABLE 4—Survey of End-Results in Fifty-Four Cases in the Orthopedic Department

Total Patients	Living	Deaths	Follow up Examination in 1933	No Follow up Examination Well Last Visit
54	46	8	41	5
Present status of lesion in 41 patients				
Entirely healed clinically and by roentgen examination				39
Healing incomplete recent ease under treatment				1
Clinically well but roentgenograms suggest residual infection				1
Residual deformities				
Deformity present, in 4 from secondary lesions of joints				5
None				36

the ankle, in 1 from tibia and in 1 from the fibula. There was also 1 with involvement of the elbow joint from the lower end of the humerus.

Of the 20 patients who died, postmortem examination was carried out on 10. With one exception, all the patients in this group had demonstrable septicemia. Eight had multiple abscesses, the organs usually involved were the liver, heart, kidneys, lungs and skin. All but 1 had bronchopneumonia, this was particularly extensive in the 2 patients who did not have multiple abscesses. However, bronchopneumonia is observed rather commonly at postmortem examination, and in 1 case the pneumonia was considered terminal. Two of the patients with multiple abscesses had vegetative endocarditis.

*Final Prognosis*—The most interesting side of this study has been a recent follow-up examination of 54 patients treated in the orthopedic service. The present status of 41 of the 46 who recovered was recently determined by physical and roentgen examination (table 4). Many of those examined had had osteomyelitis from ten to twenty years previously.

Only 2 patients in the entire group showed evidence of the persistence of osteomyelitis. The case of 1 child, aged 2 years, in whom

osteomyelitis can be localized in experimental animals by injury to the bone after the injection of organisms into the blood stream. These experiments suggest that trauma may well be a factor in precipitating osteomyelitis in the presence of bacteremia or septicemia.

The clinical history of trauma is frequently unreliable as pain in an extremity is often ascribed to vague injuries. Sixteen or 17 per cent (table 1) of the patients had a history of local injury of minor degree, of these, 10 did not have a history of antecedent infection.

#### BACTERIOLOGY

The usual conception of osteomyelitis is that it is an infection due to *Staphylococcus aureus*. This conception is true of the condition in older children. *Staph aureus* was the offending organism in 91 per cent of a series of cases in older children (from 2 to 12 years) observed in this hospital, however in the group of infants *Streptococcus haemolyticus* was by far the predominant organism.

Cultures were made in 76 of the 95 cases (table 2). This included not only cases in which a positive culture was obtained from material taken directly from the bone involved but also, in a few instances cases in which there was definite clinical and roentgenographic evidence of osteomyelitis and a positive culture of the blood was obtained although the bone itself was not exposed by operation. In 48 cases or 63 per cent, there was a streptococcic infection, in nine tenths of these the organism was *Str haemolyticus*. *Staphylococcus* was found to be present in 22 cases or 30 per cent of these. *Staph aureus* was present in all except 2, in which *Staphylococcus albus-haemolyticus* was present. There were 3 cases in which *Pneumococcus* was present and 1 in which the gonococcus was identified by smear and by culture.

It is interesting to observe that in the cases with a history of antecedent infection of the respiratory tract the osteomyelitis was due to *Streptococcus* in 22 of the 25 cases in which a culture was made. *Pneumococcus* was present in 2 cases and *Staph aureus* in 2. In other words, the probability of the osteomyelitis being streptococcic, possibly pneumococcic, is certainly suggested in any case in an infant in which an antecedent infection of the respiratory tract was present.

Of the cases in which there were preceding cutaneous lesions, the organism was *Staphylococcus* in 8 and *Streptococcus* in 5, this is not a large preponderance of staphylococcic infection but when one considers that in only 22 cases of the total group was *Staphylococcus* obtained, it increases the relative significance of the figure.

*Organism Related to Mortality*—In the 48 cases in which a culture of *Streptococcus* was obtained there were 10 deaths a mortality rate of 20 per cent (table 2). In the 22 cases in which a culture of *Staphylo-*



window was made through the cortical bone, though in a small percentage drill holes were made for drainage

2 Thirty-four cases in which indirect drainage of the bone was done without surgical attack on the bone itself In the majority of these the periosteum had ruptured at the time of operation and simple surgical drainage of the secondary abscess was performed In 8 cases the periosteum was incised before it had ruptured, and in all but 2 pus was obtained

In the other group, 11 cases, nonoperative treatment was carried out by election on 8 patients, and the other 3 were moribund on admission and died soon thereafter

*Surgical Treatment*—Direct Surgical Attack on the Bone In general the treatment in the cases in which a direct decompression of the marrow spaces was carried out through a window of moderate size in the bone represents the usual conception of the ideal treatment of osteomyelitis There might be criticism because of the interval of time that was allowed to elapse from the onset of the disease to the operation in many instances In general, it is somewhat longer for this group than for older children, for whom the diagnosis can be made more easily and examination is made earlier in the course of the disease However, in answer to this criticism, those operated on after a relatively long interval did as well as those operated on very early, as regards both the immediate and the final result, in fact, the 2 patients having the longest and stormiest postoperative convalescence underwent a surgical procedure on the first and second day, respectively, after the onset

Case 1 is representative of the cases in which drainage was accomplished by a window in the bone

*CASE 1—Osteomyelitis in the lower end of the right femur*

G C, a girl aged 1 year, was admitted to the hospital on April 7, 1932, with a complaint of irritability and pain in the right lower extremity of four days' duration Her health previously had been good There was no history of immediate antecedent infection or injury

Examination disclosed a moderately ill child, with a diffuse swelling of the lower third of the thigh, with tenderness maximal at the lower end of the femur A relatively normal range of painless motion was possible at the knee joint The roentgenograms of the femur were normal except for edema of the soft tissues The temperature was 103.4 F The white blood cell count was 27,000 per cubic millimeter

At operation a window was made in the lower end of the femur The wound was packed open with gauze impregnated with petrolatum, and the extremity was immobilized in a plaster hip spica The organism present was *Str. haemolyticus*

A roentgenogram made postoperatively, on May 5, showed mottled rarefaction of the lower third of the femur, with periosteal reaction about the lower half of the shaft

gave negative results Six of the ten patients with streptococcic septicemia died, and 4 of the 6 with staphylococcic septicemia died

*Comment*—The outstanding frequency of streptococcic infection in cases of osteomyelitis in young children is possibly due to a greater general susceptibility to such infection in infants and is, in part an indication of the types of infection which they contract For example, sepsis of the joints of infants is likely to be streptococcic, increasing numbers of cases of staphylococcic infection being observed in the later years This suggests that the infant has relatively less natural immunity to certain strains of *Streptococcus* than to *Staphylococcus* and that from repeated infection an acquired immunity develops to *Streptococcus*, which becomes more effective as the infant grows older, this is not so outstanding with *Staphylococcus* This suggestion is enhanced by the fact that the mortality rate from streptococcic osteomyelitis is much higher in infants under 6 months of age than in older children

#### SYMPTOMATOLOGY AND DIAGNOSIS

The early clinical picture of acute osteomyelitis in infants is not essentially different from that seen in older children, namely acute illness with the general systemic manifestations provoked by sepsis together with local pain and sensitivity of the involved part (see the reports of cases) The severity of the onset and subsequent illness is as variable in this group as in older children To illustrate this variability we have classified the cases in this series according to the severity of the condition at the time of admission to the hospital into four divisions (1) those in which the patient was not severely ill 15, (2) those in which the patient was severely ill but not critically so, 26, (3) those in which the patient was critically ill 20, and (4) those in which the patient was moribund and the prognosis was considered totally bad, 13 To clarify this classification further, we should comment that in group 1 some of the patients had a temperature as high as 102 F and a white blood cell count as high as 20,000 per cubic millimeter of blood

Of the local findings, protection and muscle spasm were recognized earliest Tenderness at the metaphysis is not a reliable sign at this age, though usually with patience definite information may be obtained Local edema comes on more rapidly in infants than in older persons and is much more diffuse, in fact, the entire extremity may be swollen from a process involving a single bone, even though the infection has not perforated the periosteum Although ordinarily the swelling is maximal at the site of the lesion, frequently it is not circumscribed enough to define the area involved

*Differential Diagnosis*—The differential diagnosis may be difficult before changes occur in the bone which are visible in roentgenograms The more common confusing possibilities are sepsis of the joint and

motting of the lower third of the femur with considerable subperiosteal new bone (involucrum), there was no gross sequestration.

Although this was the usual picture, not all in this group had such an uneventful course and in 2 cases there was extensive sequestration of the type seen in older persons. Case 2 is an example.

*CASE 2—Osteomyelitis of the upper shaft of the left femur*

J. M., a boy aged 1 year and 1 month, was admitted to the hospital on Dec 27, 1927, with a complaint of acute illness for four days and pain in the left thigh for twenty-four hours. There was a history of a boil one month before the onset and of a fall on the day of the onset without apparent injury.

Examination disclosed a severely ill child, with slight swelling of the upper one third of the thigh and marked tenderness, maximal over the upper end of the femur. Gentle motions of the hip joint were not particularly limited. The temperature was 104 F. The white blood cell count was 22,000 per cubic millimeter. A blood culture showed *Staph aureus*. Roentgenograms gave negative results.

At operation on the day of admission a window was placed in the upper portion of the femur below the greater trochanter. Pus was present beneath the cortex. The wound was packed open with petrolatum gauze. Immobilization was accomplished in a plaster spica. The organism isolated from the wound was *Staph aureus*.

Roentgenograms made postoperatively on Jan 30, 1928, showed extensive rarefaction of the proximal half of the shaft of the femur, with a large involucrum surrounding the bone throughout its length. On May 11 roentgen examination revealed the involucrum to be even more extensive, with definite sequestration of a large part of the shaft. The wound continued to drain.

Sequestrectomy was carried out in June 1929. The sinus closed in April 1930, two years and four months after the onset.

Final examination on Feb 3, 1933, five years and two months after the onset, revealed the child to be entirely well. Roentgenograms made at this time showed marked thickening of the shaft, but there was no other evidence of residual infection (fig 2).

This child was likewise operated on on the day of admission, which was possibly four days after the onset, although there had been symptoms referable to the local area for only twenty-four hours. The window was farther from the greater trochanter than the ideal site, but pus was obtained, the wound was packed open and the part was temporarily fixed in plaster, although afterward the extremity was only intermittently immobilized, and dressings were changed frequently.

The large sequestrum, the slowly healing sinus and the residual thickening suggest the usual picture of osteomyelitis in older persons rather than that seen in infants. It was most unusual in this series. In the only other patient who showed an extensive sequestrum, a window was made on the second day after the onset and the organism was likewise *Staph aureus*. One might suspect that the formation of a sequestrum was typical of staphylococcic osteomyelitis even at this age, except that in only 3 of the 22 cases in which this organism was present was a sequestrectomy necessary. By comparison, in only 3 of the 48 cases of streptococcic osteomyelitis was a sequestrectomy needed and

## PROGNOSIS

*Immediate Prognosis*—Of the 82 patients with acute osteomyelitis, 18 died—a mortality rate of 22 per cent. Seventy-one of the 82 patients were operated on, 11 were not. Of the latter group, 3 patients were moribund when they were admitted to the hospital and died almost immediately. Fifteen deaths occurred in the cases in which operation was performed (table 3).

*Period of Hospitalization*—The average period of hospitalization of the patients who recovered was six weeks. In this connection we should point out that frequently the patient was kept in the hospital until the sinus had closed or at least needed no further packing. In only 6 instances was the patient admitted more than once, and in 3 this was for the care of secondary lesions of joints.

TABLE 3—*Immediate Prognosis*

	Number of Patients	Deaths	Mortality, per Cent
Acute osteomyelitis	82	18	22
Chronic osteomyelitis	13	2	15
Total	95	20	21
Average period of hospitalization			6 weeks
Average duration of sinus			12 weeks
Reurrences			2 cases
Sequestration			6 cases

*Duration of the Sinus and Recurrences*—The average time from the onset until the sinus had healed was twelve weeks, although by omitting 3 cases this average could be reduced to eight and one-half weeks. In all but 3 of the 56 cases of acute osteomyelitis in which operation was performed, healing was complete in four months, in 31 of the 56 healing was complete at the end of two months.

Once the sinus was healed, in only 2 cases was there a recurrence. In both instances drainage persisted for two weeks, and the sinus closed voluntarily and remained healed.

*Sequestration*—Sequestration was comparatively rare. In only 6 cases was sequestrectomy necessary, these were the only cases in which gross sequestrums were present although in 2 cases of osteomyelitis of the neck of the femur there was a gradual absorption of the head after the sinus was healed. As previously mentioned, roentgenograms made during the course of the disease frequently suggested that sequestration would occur, but it did not materialize.

In only 20 of the 95 cases was there more than one operation, and in 10 of these the operation was for a lesion other than the primary osteomyelitis.

consisted merely of making an incision into the secondary abscess, packing it wide open with petrolatum gauze and immobilizing the part. The following cases may be considered in this group.

CASE 3—*Osteomyelitis of the right ulna*

R. L., a boy aged 1 year and 8 months, was admitted to the hospital on July 16, 1932, with a complaint of acute illness and pain in the right upper extremity of five days' duration. His health previously had been good, but he had had a rather severe infection of the respiratory tract for the two weeks preceding the present illness. The arm had been immobilized for four days immediately preceding admission.

Examination revealed the child to be moderately ill, with a marked, diffuse, tender swelling from the wrist extending upward beyond the elbow. Motions of the elbow and wrist joints were normal. The temperature was 103.6 F. The white blood cell count was 23,000 per cubic millimeter. Roentgenograms gave negative results, except for evidence of swelling of the soft tissues.

At operation the abscess was drained (the bone was not explored). Immobilization was effected. A culture of material from the wound showed *Str. haemolyticus*.

On August 16 the roentgenologists reported considerable destruction of the ulna with a large amount of irregular bone surrounding it. The shaft seemed to be forming a sequestrum.

The wound healed in six weeks.

Final examination on Feb. 27, 1934, eighteen months after the onset, revealed the lesion to be entirely healed. The roentgenogram at this time showed the bone to be apparently normal (fig. 3). The sequestrum did not materialize.

CASE 4—*Osteomyelitis of the lower end of the left radius*

E. L., a girl aged 1 year, was admitted to the hospital on Nov. 20, 1932, with a complaint of an acute illness of twenty-four hours' duration, associated with pain and swelling of the left forearm. The child's general health had been good previous to the present illness except for an infection of the respiratory tract during the preceding week.

Examination revealed the child to be quite ill, with tender swelling of the distal half of the left forearm. Movement of the wrist joint was not particularly painful. The temperature was 104.2 F. The white blood cell count was 29,400 per cubic millimeter. A roentgenogram showed no abnormalities.

At operation on November 21, the abscess was drained, the wound was packed with petrolatum gauze and the arm was immobilized in plaster. A culture of material from the wound showed *Str. haemolyticus*.

On December 23 the roentgenologists reported that the radius showed a considerable amount of generalized mottled absorption of practically the entire shaft, with a moderate amount of subperiosteal new bone surrounding the shaft.

The sinus healed two months after the onset. In February 1934, fifteen months after the onset, the forearm was apparently normal on both clinical and roentgen examination (fig. 4).

CASE 5—*Osteomyelitis of the upper end of the left tibia*

H. F., a boy aged 4 months, was admitted to the hospital on Dec. 28, 1932, with a complaint of an acute illness of five days' duration, associated with pain in the left leg. The day before admission to the hospital the patient would not move his leg, and the mother noted that it was swollen. His health, previous to a per-

in November 1932 there developed acute osteomyelitis of the neck of the femur, the ilium and the fibula associated with staphylococcal septicaemia is subsequently discussed as case 7. The other patient had acute osteomyelitis of the femur in 1927 and although she has been free from symptoms since that time with unlimited activity roentgenograms suggest the presence of a smoldering lesion. In 2 cases a recent examination showed considerable residual thickening of the bone but no clinical or roentgenologic evidence of activity (case 2). Roentgenograms in the other cases showed the lesions to be healed.

There were 5 cases with resultant deformity. In 4 the defect resulted from secondary sepsis of the joint; in the other, after a too extensive operation very early in the course of the disease the radius regenerated poorly, with ankylosis to the ulna. Of the cases of deformity due to involvement of the joints in 2 the deformity was of the hip with absorption of the head of the femur; in 1 of the knee with ankylosis and in the other of the elbow. The last-mentioned case was one of recent involvement, there was little residual deformity and the condition is still improving.

There was some tendency for the involved bone to be a little shorter than its fellow in 5 cases, but in no instance except when the joint was involved was the difference over  $\frac{1}{2}$  inch (1.2 cm). There were no cases of residual lengthening.

The present status of the younger patients forms a striking contrast to the usual picture of osteomyelitis. We have been able to determine the present state of 41 of the 46 patients now living who were treated in the orthopedic service; in only 2 cases was there any suggestion of the presence of residual osteomyelitis: 1 a recent case in which there was healing and another a case in which there were no symptoms. In all but 1 case the deformity was due to involvement of the joint. In many cases of extensive destruction during the acute process one could find evidence of the original lesion in the roentgenograms with difficulty and in several not at all.

This contrast to the picture of the disease in older children is further emphasized by the relatively brief duration of the disease in infants with rapid healing, infrequent sequestration and rare recurrences.

#### TREATMENT

For consideration of the treatment of acute osteomyelitis we have classified the cases in two groups: 71 cases in which there was surgical intervention and 11 cases in which treatment was nonoperative. The first group may be subdivided as follows:

1. Thirty-seven cases in which drainage of the bone was done by a surgical procedure directly on the bone. In the majority of these a

sistent infection of the respiratory tract which had developed one month before had been good

Examination revealed the child to be critically ill, with a diffuse, tender swelling of the leg, maximal just below the knee. The temperature was 106.2 F. The white blood count was 30,000 per cubic millimeter. A roentgenogram showed nothing abnormal.

At operation the abscess was drained, the wound was packed with petrolatum gauze and the leg was immobilized in a plaster cast. Culture from the wound showed *Str. haemolyticus*.

A roentgenogram made on Jan. 10, 1933, showed irregular destruction throughout the shaft of the tibia, with a surrounding involucrum extending the length of the bone. There was slight anterior and lateral displacement of the upper epiphysis of the tibia.

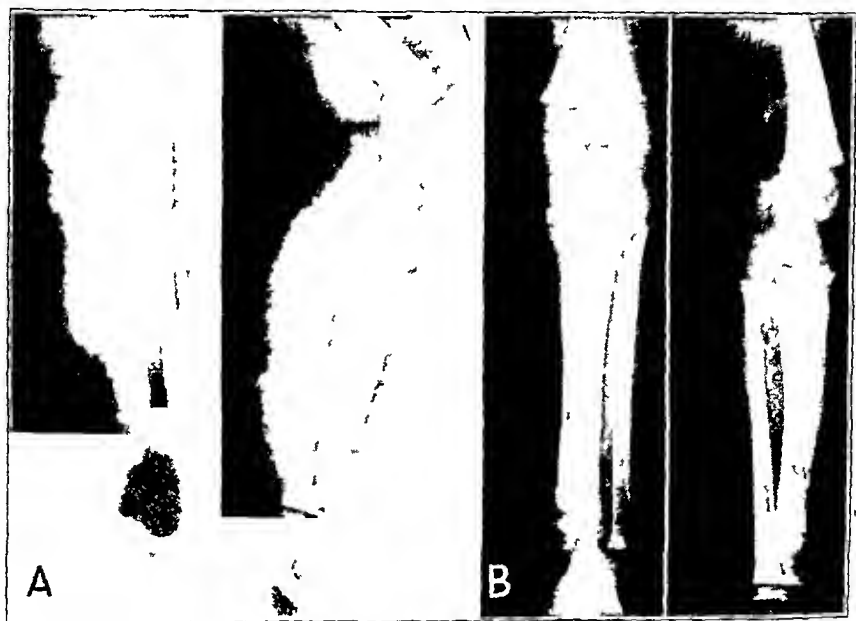


Fig. 5 (case 5)—*A*, made three weeks after the onset, shows marked destruction of the shaft of the tibia, with displacement of the upper epiphysis. *B*, made one month later, shows remarkable healing in a brief period. Note the suggested narrowing of the epiphyseal line. Treatment was limited to drainage of the abscess.

The wound healed in three months.

Roentgenograms made on February 20, three months after the onset, showed healing, with no evidence of sequestration. There was a suggestion of narrowing of the epiphyseal line (fig. 5).

In all 3 of the patients localization had occurred, and the pus had ruptured through the periosteum. The surgical procedure consisted merely of draining the abscess in the soft tissue adequately and of immobilizing the part. All the patients were severely ill at the time of admission, and the roentgenograms made subsequently in each case

The patient was discharged from the hospital on June 3. The sinus healed two and one-half months after the onset.

Final examination in October 1933 (eighteen months after the onset) showed the extremity to be normal in all respects except for the postoperative scar. Roentgenograms at this time showed little evidence of the former lesion (fig 1).

The child was moderately but not critically ill. She was operated on the day after she was admitted to the hospital, which was five days after the onset. There was no pus immediately beneath the periosteum.

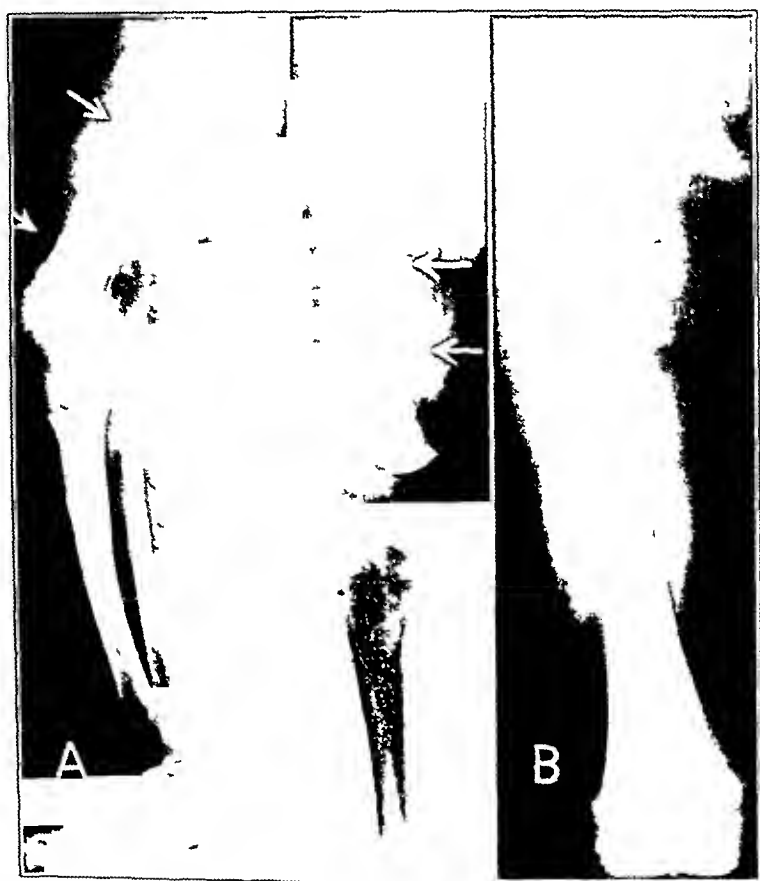


Fig 1 (case 1) — *A*, made one month after the onset, shows mottled destruction of the lower third of the femur, with subperiosteal new bone about the lower half of the shaft. *B*, made one and one-half years later, shows little evidence of the former lesion. Treatment was by surgical intervention, a window was placed in the bone adjacent to the epiphysis.

but a moderate-sized window in the cortex revealed pus. The wound was packed open with petrolatum gauze, and the part was immobilized in a hip spica which was bivalved. Dressings with replacement of the petrolatum gauze were done at weekly intervals. There was uneventful and rapid recovery, and although the early roentgenograms showed



count was 22,000 per cubic millimeter. The reaction to tuberculin was negative. Roentgenograms showed an area of absorption in the neck of the femur.

Nonsurgical treatment was instituted, with immobilization by means of a wire splint with the leg in abduction. Roentgenograms made on Jan 19, 1932, showed rarefaction of the neck of the femur, with a subperiosteal deposit of new bone about the upper third of the shaft of the femur.

Final physical examination on Feb 24, 1933, fifteen months after the onset, showed the extremity to be normal. Roentgenograms made at this time showed complete healing, with slight residual thickening of the neck. The organism was not known (fig 6).

The 5 mildly ill patients who were treated by immobilization recovered completely as did the patient in case 6. The following case is one in which a critically ill patient was treated without surgical intervention.



Fig 6 (case 6)—A shows an area of destruction in the neck of the femur with mild subperiosteal reaction for half the length of the shaft. B, made thirteen months later, shows the lesion completely healed. Treatment was by immobilization, without surgical intervention.

#### CASE 7—*Osteomyelitis of the neck of the left femur*

A M., a boy aged 2 years, was admitted to the hospital on Nov 4, 1932, with a complaint that three days before pain had developed in the left lower extremity, associated with a rapidly developing acute illness. The past history was significant in that the patient had recently had several boils, and two days before the onset of the present illness he had fallen on a furuncle of the right buttock, rupturing it.

Examination revealed a critically ill, rather stuporous child, with his left hip held in flexion by muscle spasm. There was a suggestion of fulness over the capsule of the hip joint. Tenderness could not be definitely localized. When the extremity was handled with care a large amount of relatively painless motion at the hip joint could be obtained and the flexion deformity could be reduced. The

there were no sequestrums of the size seen in the 2 cases reported Staphylococcic osteomyelitis even at this age seems more likely to produce extensive sequestration than streptococcic osteomyelitis

**Drainage Without Surgical Attack on the Bone** The 34 cases in this group represent a less orthodox method of therapy though as mentioned by Lewis' simple incision for patients of all ages was advocated



Fig 2 (case 2) —A shows a picture of osteomyelitis as frequently seen in older children. Only in this case and in one other was this type of sequestration observed. The roentgenogram made just previous to sequestrectomy shows the sequestrum well outlined. B, made three and one-half years later shows residual scarring but no evidence of activity. There have been no symptoms for two years. The primary surgical procedure was the formation of a window in the bone four days after the onset.

bv Trendelenburg, Wilms and Sauerbruch. At the time of operation the bone was not disturbed. In the majority of cases the procedure

A roentgenogram made on January 20 showed destruction of the greater part of the head of the femur, with lateral luxation

On final examination, on March 4, 1933, the child walked with a lurch on the right, with the extremity in about 25 degrees of external rotation. Although the hip was fairly stable, there was limitation of all motions, with extension to neutral, flexion to 55 degrees and external rotation to within 15 degrees of neutral



Fig 7 (case 7) —*A*, made one month after the onset, shows extensive destruction in the neck of the left femur, with a reaction in the upper third of the shaft. There is an area of rarefaction in the ilium also. *B*, made three months later, shows considerable healing; the arrows indicate areas of destruction. *C*, made nine months later, shows the lesion in the lower end of the femur nearly healed. The upper lesion has not yet healed and is still under treatment. Treatment was by immobilization, without surgical intervention.

There was  $3\frac{1}{2}$  inch (15 cm) shortening. A roentgenogram showed absence of the head, with the neck articulating with the acetabulum (fig 8).



Fig 3 (case 3) — *A* made one month after the onset shows extensive destruction throughout the shaft of the ulna, with an irregular deposition of new bone *B* made two months later shows healing and *C* made eighteen months later shows the ulna apparently normal. Treatment was limited to drainage of the abscess.



Fig 4 (case 4) — *A* shows extensive destruction throughout the shaft of the radius and *B* the bone apparently normal fifteen months later. Treatment was limited to drainage of the abscess.

On the basis of this limited experience we do not recommend conservative treatment in all cases of osteomyelitis of the neck of the femur in patients at this age. We do recommend, however, that if the patient is carefully observed, a conservative attitude may be taken, and frequently surgical procedure may be avoided. If there is evidence that the process ruptures into the joint, the joint should be drained, or if there are other indications for operation, it should be carried out.

#### COMMENT AND CONCEPTION OF TREATMENT

In contrast with the osteomyelitis of older persons is the osteomyelitis of infants, with its relatively brief duration, infrequent sequestration and rare recurrences. To what do we ascribe these differences?

They are due in part to the fact that *Staph aureus* is less frequently present in this group. *Staph aureus* is a destructive organism whether it involves soft tissue or bone and produces sequestration more often than *Str haemolyticus* in patients of any age,<sup>6</sup> but there is not so striking a difference as there was in this series.

It is our opinion that certain anatomic and physiologic features in bones themselves are a considerable factor. Osteomyelitis in general may be considered "a cellulitis of bone," with death of tissue from the direct activity of the infection and from disturbances of the vascular supply, which seem to be in part mechanical. The necrosis causes the extensive sequestration seen in dense cortical bone.

In the bones of infants certain factors militate against this occurrence. In infancy the vascular spaces are larger and the bone is of spongy texture, even in the so-called compact portion, as suggested by Bardeen,<sup>6</sup> the bony tissue has a much larger soft tissue element and generally less rigidity. This construction allows freer communication between the marrow and the subperiosteal spaces and thus provides a mechanism for a decompression by which the pus from the juxta-epiphyseal area and marrow cavity is able to pass to the subperiosteal space. Ordinarily osteomyelitis has its origin in the metaphysis (fig 10), and Starr's<sup>7</sup> opinion was that the infection passes from there through the thin cortical bone and appears subperiosteally. It may be seen in figure 9 that although the cortical bone is thinner at the metaphysis than elsewhere in older children, it is particularly thin in

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6 Bardeen, C. R., Kerbel, F., and Mall, F. P. *Manual of Embryology*, Philadelphia, J. B. Lippincott Company, 1910.

7 Starr, C. L. Acute Hematogenous Osteomyelitis, *Arch Surg* 4:567 (May) 1922, Acute Infections in Bone, in Robert Jones Birthday Volume, London, Oxford University Press, 1928, p. 183.

suggested extensive sequestration although in no instance did this occur. The sinuses healed rapidly, as did the bone.

These cases are representative of the group in which drainage was accomplished without attacking the bone although also in this group are those cases in which the periosteum was incised either before or after the presence of gross pus. Case 5 is reported because the early roentgenogram showed displacement of the epiphysis (the child's extremity was not protected for the five days previous to admission), and the final one suggested some residual narrowing of the epiphyseal line.

A statistical comparison of those cases in which treatment by drainage of the abscesses of the soft tissue was employed and those in which direct drainage of the bone was used has shown little difference in either immediate and final outcome. In the amount of bone involved, as viewed by subsequent roentgenograms, metastatic lesions and the interval for the sinus to heal, no differences were noted. Of the 37 patients treated by operation on the bone, 7 died; of the 34 treated by drainage of abscesses of the soft tissues, 8 died. However, it is difficult to make a direct statistical comparison unless contrasting operations are carried out on patients with a similar condition, and only more recently has this been done. For example in some of the cases in which drainage of the abscess alone was carried out, the patient was in such poor condition that no more could be done. This was naturally unfavorable to the statistics for the group.

It is interesting that there was only 1 case in the group in which simple drainage was used in which it was necessary to perform a sequestrectomy. In this case operation was performed on the second day of the disease, and the periosteum was incised before localization had occurred, subsequently it was necessary to remove a sequestrum the size of a pea. On the other hand, in case 5, with similar treatment, there is some residual narrowing of the epiphyseal line, and it will be necessary to follow this case to see whether or not growth is in any way affected.

*Nonsurgical Treatment*—Of the 8 patients who by choice were treated without surgical intervention, 2 were critically ill, with cultures of the blood showing, respectively *Str. haemolyticus* and *Staph. aureus*, 1 was moderately ill, and 5 were mildly ill. The following case is representative of those of the mildly ill patients.

*CASE 6—Osteomyelitis of the neck of the right femur*

M. M., a girl aged 1 year, was admitted to the hospital on Nov. 21, 1931. Ten days previously the child became irritable and feverish and refused to walk. She was not particularly ill, but all motions of the hip were painful. There was only moderate muscle spasm. The temperature was 100.6 F. The white blood cell

examination of the involved bones. What necrotic bone there is is rapidly absorbed by a process of autolysis (fig 12). Incidentally, osteoclasts are conspicuously infrequent where this process is taking place. The formation of new bone in the process of healing is remarkably rapid in infants. This is seen not only in the roentgenograms but particularly in microscopic sections of involved bone in which as soon as a week after the onset subperiosteal new bone may be noted in many instances (figs 10, 11 and 12). In other words, not only is the dead



Fig 10—Photomicrograph of the lower end of the femur adjacent to the metaphysis in a 1 month old infant, showing an osteomyelitic process of two weeks' duration. Note the necrosis and beginning absorption of the trabeculae (*d*), the thin cortical bone (*b*), areas of cellular infiltration of the acute inflammatory type (*e*) and the surrounding subperiosteal new bone (*f*). Hematoxylin and eosin, approximately  $\times 30$ .

bone rapidly absorbed, but the process of healing is equally rapid. This combination of a natural method of decompression with the additional factors of rapid absorption of the necrotic bone and equally rapid healing would seem to serve as an explanation for many of the differences between the disease of infants and that of older persons.

temperature was 106 F the pulse rate was 180 and the white blood cell count was 23,000 per cubic millimeter Repeated cultures of the blood yielded *Staph aureus*

At the time of admission the diagnosis was not definitely made, though osteomyelitis of the neck of the femur was suspected

Nonsurgical treatment was instituted, with immobilization by traction and general systemic support The temperature progressively approached normal Improvement was so marked that by the time the diagnosis could be made definitely, continued conservative therapy was indicated

A roentgenogram made on November 14, ten days after admission, showed a slight amount of irregular erosion of the neck of the femur adjacent to the epiphyseal line Lesions were demonstrated in the left fibula as well as in the right ilium

The temperature was normal from the fourteenth day after admission, except on one occasion, when following removal of traction there was immediately a flare-up of fever, with subsidence when the traction was replaced

A roentgenogram made on Jan 23, 1933, the first which included the lower end of the right femur, showed an area of rarefaction adjacent to the distal epiphysis, the other lesions were smaller and less distinct A roentgenogram made on February 15, fourteen weeks after the onset, showed further healing, and at that time the patient was given a non-weight-bearing brace and was discharged from the hospital

Following overactivity at home he returned on March 23, with a temperature of 103 F and marked muscle spasm with limitation of all motions of the hip The white blood cell count was 15,600 A culture of the blood gave negative results Traction was applied to the extremity The muscle spasm rapidly disappeared, and there was subsidence of the temperature to normal by the fifth day after admission The patient was discharged in a hip spica on April 20, one month after admission

The last roentgenogram made, in August 1934, showed the lesion of the femur to have decreased in size, but it was not healed completely All motions of the hip were painless The area in the ilium was still visible in the roentgenogram, although at no time had the patient had symptoms referable to this area (fig 7)

The following case in which osteomyelitis of the neck of the femur was treated by surgical intervention is reported for contrast with case 7

#### CASE 8—*Osteomyelitis of the neck of the right femur*

H P, a boy aged 1 year and 2 months, was admitted to the hospital on Dec 9, 1929 The onset, on November 14 was marked with a temperature of 103 F and pain in the right thigh The symptoms continued until the time of admission The child was not particularly ill but protected his right hip, which showed a deformity of 45 degree flexion, with all motions painful and a suggestion of distention of the capsule of the hip joint The temperature was 100.2 F The white blood cell count was 17,000 per cubic millimeter A roentgenogram showed an area of rarefaction adjacent to the epiphyseal line

Operation was performed on December 12 A window was made in the neck of the femur by posterior incision (according to the method of Ober) There was no pus in the joint, but thick purulent material was present in the neck of the femur A drain of rubber dam was introduced The organism present was *Staph aureus* Traction was used, though not constantly, until Jan 23 1930 when a plaster spica was applied and the child was discharged from the hospital



many, though they are greatly in the minority, who advocate waiting as a general rule. The decision depends on balancing the argument between the possible danger of operating on an early diffuse inflammatory process and that of allowing an infection to progress in rigid walls, with resultant increased necrosis of bone. As far as infants are concerned, and clinically it has seemed that the age of 2 years is a flexible but fairly definite dividing line between infancy and childhood, the importance of the latter is greatly minimized. Infants have a natural method of decompression which works effectively, with sequestration a rare accompaniment. Certainly the evidence suggests that waiting for localization should do little harm.

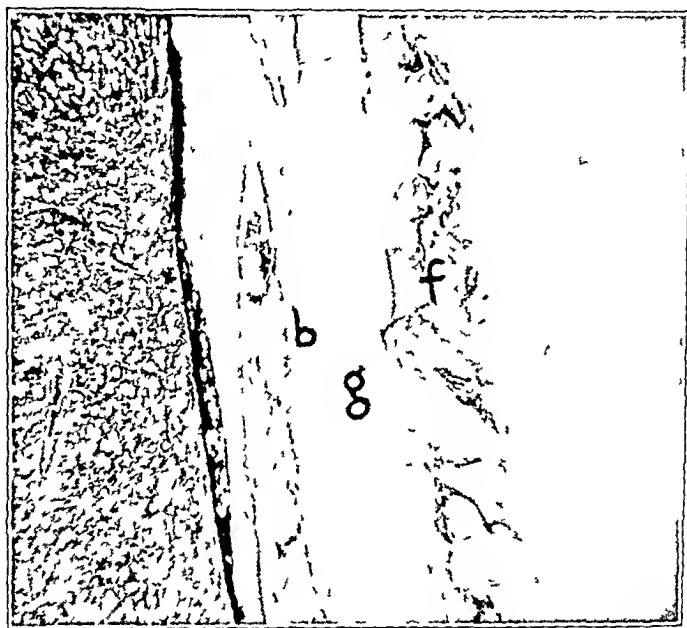


Fig 12—Photomicrograph of osteomyelitis of the fibula of nine days' duration in an infant of 1 year and 2 months. Note the autolysis of the necrotic bone (*b*) as surrounding subperiosteal new bone (*f*) is laid down. The area indicated by *g* is an artefact, i. e., separation in preparation. Hematoxylin and eosin, approximately  $\times 30$ .

This is fortunate, for the accurate determination of the site of an early lesion in a child of this age is difficult. Without this exact determination, many needless and harmful surgical procedures may be undertaken, particularly if the child is desperately ill or there is a complicating infection of the respiratory tract.

In recent years it has not been our chief concern to operate on the patient at the earliest possible moment, particularly if the site of the lesion cannot be definitely localized or there is some contraindication to operation from the general condition of the patient. We have fol-

Case 8 is an example of those cases of osteomyelitis of the neck of the femur in which treatment was surgical. Of the 3 cases, there were slow disintegration and complete destruction of the head of the femur in 2 and in the third the patient died.

On the other hand of the 3 patients with osteomyelitis of the neck of the femur treated without operation 2 were well at the time of the last examination whereas the third (case 7) although desperately ill on admission with an extensive process, multiple lesions and *Staph aureus* septicemia showed healing though roentgenograms showed that the lesion was not completely healed. Even if the drainage of the small residuum is necessary later it should not disturb the circulation of the head of the femur. This patient's lesions healed slowly but it is to

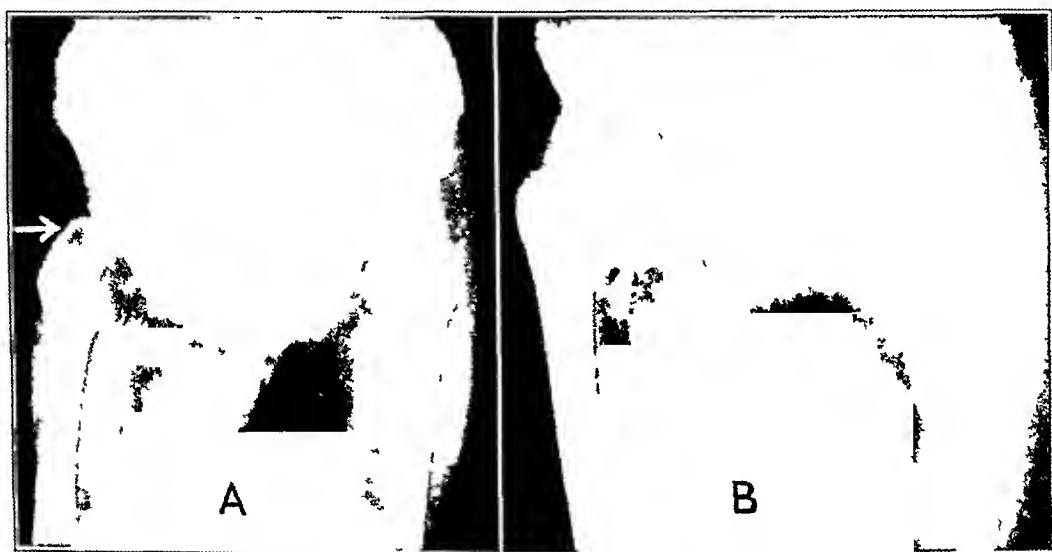


Fig 8 (case 8) —A, made three weeks after the onset and just previous to operation, shows the large area of destruction in the neck of the right femur. B, made three years later, shows complete destruction of the head of the femur. Treatment was by surgical intervention, a window being made in the bone.

be remembered that the child was at the upper limit of the age group, 2 years, and that the organism was *Staph aureus*.

A younger child with osteomyelitis of the neck of the femur and the blood showing *Str haemolyticus* almost as sick as the patient in case 7 was treated without surgical intervention. The patient is completely well.

The principal reason for treating patients with osteomyelitis of the neck of the femur by conservative means has been the difficulty in early diagnosis and of surgical attack with the added factor that so far patients so treated have done better than those who underwent operation.

reports of representative cases. Case 7 particularly illustrates the value of protecting the part, in that when the traction was removed on two occasions there was an exacerbation of the symptoms. Not only do we feel the importance of immobilization as a preoperative and immediate postoperative measure, but we consider that the part should be immobilized until the sinus has healed and there is definite evidence in the roentgenogram that the bone is healing. The only exception to this rule occurs when there is secondary involvement of the joint.

Our mortality rate has been gradually decreasing under this regimen. There has been only 1 death in the last 20 cases, and that was in an infant 3 weeks of age with primary omphalitis, *Staph aureus* septicemia, multiple visceral abscesses and involvement of six bones.

#### SUMMARY

Ninety-five cases of osteomyelitis in infants (children under 2 years) are reported on, 35 of which have been observed in the last two years. In 82 the condition was acute and in 13 chronic (i. e., duration over one month at the time of the admission to the hospital).

Osteomyelitis in infants is not a rare disease.

The mortality rate for all cases was 21 per cent. The rate was definitely higher in patients under 6 months of age (43 per cent). The rate in patients from 6 months to 2 years of age was 14 per cent.

Streptococcic osteomyelitis occurs twice as frequently as staphylococcic osteomyelitis in infants.

Antecedent infections were present in 55 per cent of the cases. Fifty per cent of the complications were infections of the respiratory tract, 25 per cent were cutaneous lesions, and the other 25 per cent were such miscellaneous infections as omphalitis and chickenpox.

When associated with infection of the respiratory tract, osteomyelitis was due usually to *Str haemolyticus*, occasionally to *Pneumococcus* and rarely to *Staph aureus*. When associated with cutaneous lesions the organism was more likely to be *Staph aureus*.

There was a history of mild trauma in 17 per cent of the cases.

In the entire group of cases of acute osteomyelitis there was a higher mortality rate with staphylococcic than with streptococcic infections, whereas in infants under 6 months of age streptococcic osteomyelitis caused a relatively higher rate.

A diagnosis is made later in the course of the disease in cases in infants than in those in older persons.

Differential diagnosis demands the particular consideration of sepsis of the joints, infection of the soft tissues and scurvy with infection elsewhere.

infants This allows in infants a free communication from the original site of the osteomyelitis to the subperiosteal space The periosteum is more loosely attached in infants and further aids in the decompression The roentgenograms of the patients in this series suggest extensive subperiosteal dissection, if one may judge from the distribution of new bone It is the usual thing for subperiosteal new bone to be evident from one half to the full length of the shaft, and, as may be seen in figure 11, this reaction extends down the shaft much farther than the involvement of the cortical bone and marrow space

Once the pus is beneath the periosteum, the periosteum may rupture without sequestration, as occurred in 26 of our cases in which operation

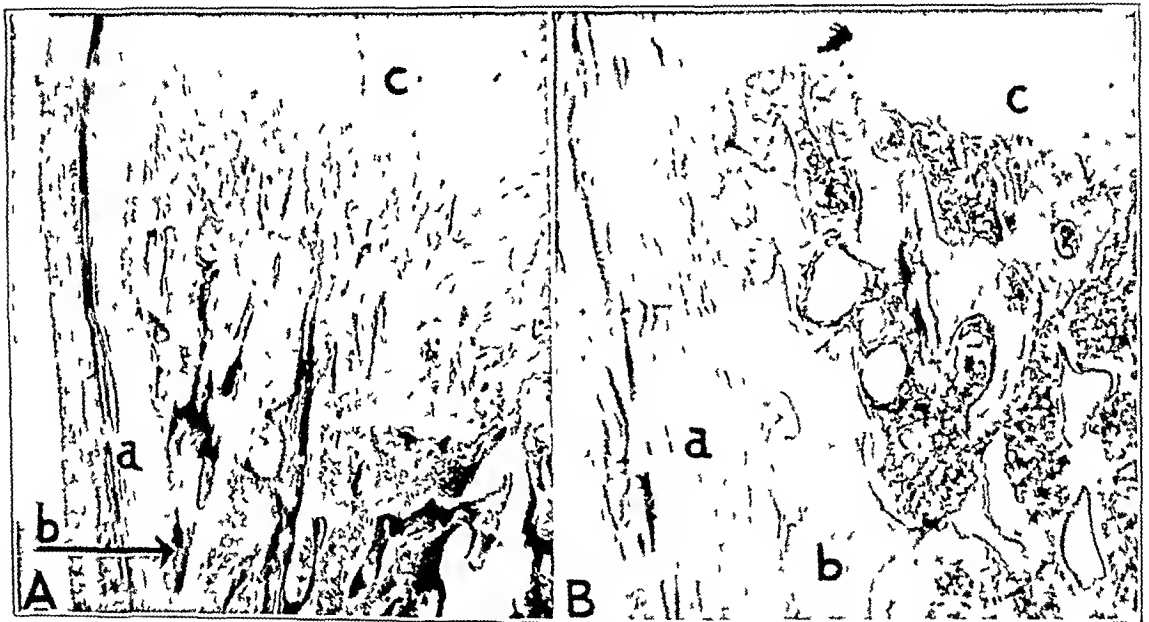


Fig 9—Photomicrograph of normal ribs at the metaphysis (*A*) in a premature infant and (*B*) in a child of 11 years In *A* note that little cortical bone (*b*) is present at the metaphysis, allowing a rather direct communication between the marrow and the subperiosteal spaces The cortical bone in the remainder of the shaft shows relatively larger haversian canals than are seen in older persons There is a contrast with *B*, in which there is a relatively thick layer of cortical bone (*b*) at the metaphysis, although even at this age the cortical bone at the metaphysis is relatively thin as compared with the remainder of the shaft In this illustration *a* indicates periosteum, *b* cortical bone, and *c* the epiphyseal line Hematoxylin and eosin, approximately  $\times 30$

was not performed until after the periosteum had ruptured In other words, there is an orderly decompression by nature without gross sequestration except in rare instances

Further factors which seem to explain the rapid healing of the lesions and the infrequency of sequestration are suggested by histologic

The therapy we have adopted is based on the following considerations

(a) The care of the patient rather than the osteomyelitis is the important consideration

(b) Surgical intervention at an early period in the disease is not essential. If the condition of the patient is satisfactory and the lesion can be located definitely before operation, an operation may be performed

(c) If surgical intervention is contraindicated by the general condition of the patient, the part should be immobilized and supportive treatment should be given. Delay does not increase the danger of sequestration, which is remote in any instance, and particularly so if the offending organism is *Streptococcus*

(d) If an operation is performed on the bone it should not be extensive

(e) Adequate drainage of the fluctuant abscess in infants, without operation on the bone seems to give as satisfactory results as a more extensive procedure. If the abscess is drained a prolonged search for the lesion in the bone should never be made

(f) Packing the wound open with petrolatum gauze combined with immobilization in a plaster cast is a desirable method of treatment. The cast should be bivalved to allow for dressings. The first dressing should not be made until ten days after the operation, thus allowing granulation tissue to line the wound. At that time dressing can be done painlessly. Dressings are done at weekly intervals thereafter with replacement of the petrolatum gauze

(g) The part should be immobilized until the wound has healed and there is evidence of healing in the roentgenogram

Since this therapy was instituted our mortality rate has greatly decreased. There has been only 1 death in the last 20 cases

#### CONCLUSION

Osteomyelitis of infants differs greatly from osteomyelitis of older children, not only in many clinical features but also in many principles of therapy

NOTE—Since this paper was prepared, we have seen an article by Paschla<sup>9</sup> in which the author pointed out differences between the osteomyelitis of infants under 1 year and that of older children. He contrasted the pathologic process and certain clinical features of the

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<sup>9</sup> Paschla, G. Die Besonderheiten der Osteomyelitis im frühen Kindesalter, *Monatschr f Kinderh* 55 280, 1932

Ordinarily a patient with cellulitis generally speaking does better when the process is allowed to localize than when it is incised early, particularly if the infection is streptococcic. On this basis there are

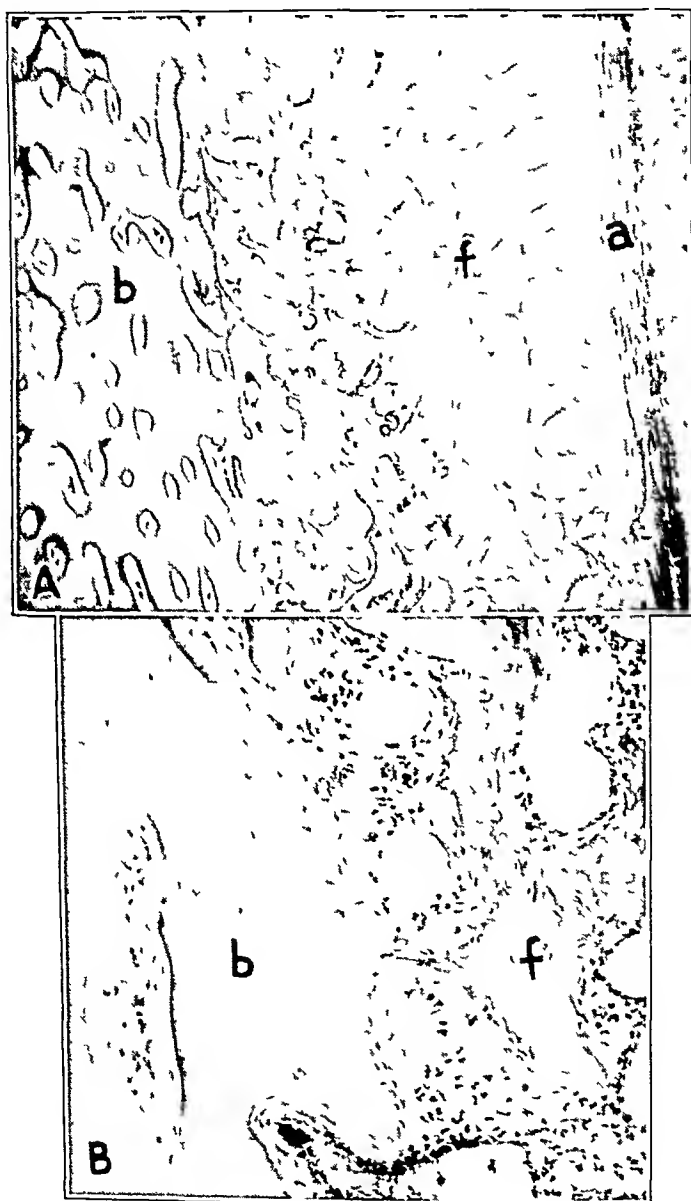


Fig 11—*A* is a photomicrograph of the midshaft of the same bone as that seen in figure 10. Note the extensive layer of subperiosteal new bone (*f*) surrounding the living bone of the shaft (*b*). The subperiosteal new bone extends much farther down the shaft than the involvement of the cortical bone. Hematoxylin and eosin, approximately  $\times 30$ . *B* is the same as *A* in higher magnification (approximately  $\times 83$ ). Hematoxylin and eosin.

# IMMUNOLOGY OF OSTEOMYELITIS

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Hematogenous osteomyelitis is considered a surgical problem. It is our belief that antecedent to the presenting surgical problem of acute osteomyelitis is the fact that susceptibility to this infectious process depends on the presence or the absence of immunologic defenses in the host. These defenses are the preeminent factors in susceptibility, acuteness and chronicity, and they may determine the mortality and the tendency to recurrence.

In the hands of experienced surgeons operative technic has reached a supreme degree of perfection. No one questions that surgical intervention for osteomyelitis is frequently a life-saving procedure and markedly shortens the course of the chronic infection. In the face of these facts the incidence of osteomyelitis remains the same, and the percentage of recurrences in properly handled cases still remains high. This evidence warrants a study of the immunology of this infectious process in an attempt to throw some light on the problem of susceptibility and of recurrence.

This paper is confined to a consideration of hematogenous osteomyelitis. In over 90 per cent of the cases the staphylococcus is the invading organism and is obtained in pure culture. Pigment-producing strains predominate. Let it be recalled that in every case osteomyelitis is at its inception a bacteremia. The blood in a majority of cases eventually sterilizes itself, with the localization of the invading bacteria in certain bones. If the infection is virulent and the body defenses are inadequate, multiple bones may become involved with a recurrence of bacteria in the blood.

When one attempts to estimate accurately the percentage of deaths due to acute osteomyelitis, a wide discrepancy of individual statistics is noted. However, a compilation of statistics gathered from various competent observers places the mortality at approximately 10 per cent. From the registration area of the United States during the years 1930, 1931 and 1932, 3,160 deaths were reported from osteomyelitis<sup>1</sup>. It is significant that 90 per cent of the deaths occur within the first two weeks

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From the Contagious Service of the Kansas City General Hospital, in collaboration with the Department of Orthopedic Surgery.

<sup>1</sup> Bureau of the Census, Mortality Statistics, 1930, 1931, 1932, Washington, D. C., Government Printing Office.

lowed the practice of immobilizing the part, usually with poulticing, and of giving general supportive therapy. Almost without exception the children have improved following this regimen. Once the site of the lesion is definitely recognized and the child is considered a good surgical risk or at least the possibility of improving his condition for operation is no longer present, one should consider operation. However, in many instances in our series we deliberately waited until the abscess became localized and fluctuation was palpable before carrying out a simple drainage of the abscess, without any operative procedure on the bone. It being remembered that the immediate danger of the acute disease is the foremost consideration with young patients, this attitude allows a minimal amount of surgical trauma and permits the time of operation to be chosen with full consideration of the patient's condition. The patients in these cases have done very well, and the course compares most favorably with that in the others. In none of them has there been sequestration or has the sinus failed to heal within four months. Neither has the incidence of sepsis of the joints been greater, although more cases must be observed to determine this point with finality.

Whether this method of allowing localization of the abscess with simple drainage is preferable to making a window in the bone at an earlier time, we cannot say. In any event, if the abscess is drained a prolonged search for the lesion in the bone should not be made nor should the operative procedure be complicated in order to make a window in the bone.

The way in which the infection has been taken care of in the cases in which conservative treatment was followed further aids one's conception of the disease in infants. Mild, acute osteomyelitis may take care of itself without drainage following immobilization, occasionally this is true in cases in which the patient is severely ill.

*Postoperative Care*—It is our usual practice to pack the wound with petrolatum gauze and immobilize the part with a plaster cast which is bivalved. The wound is not dressed until granulations have formed, so that the dressing may be accomplished without trauma, in other words, from seven to fourteen days after the operation. Dressings are then done at about weekly intervals, with replacement of the petrolatum gauze, until it can no longer be introduced. At this time a rubber tissue dressing is used which keeps the margins of the wound moist, facilitates drainage and obviates too early closure of the external orifice of the sinus. In our experience this regimen is less odoriferous and more conducive to prompt healing than the unmodified regimen of Orr<sup>8</sup>.

*Immobilization*—An essential part of our preoperative and post-operative regimen is immobilization of the part, as may be seen in the

<sup>8</sup> Orr, H. Winnett. Osteomyelitis and Compound Fractures, St. Louis, C. V. Mosby Company, 1929.



Van de Velde <sup>2</sup> first demonstrated that certain strains of staphylococci produced leukocidin, which in all probability is identical with the exotoxin and which has properties both to hemolyze blood and to necrose tissue. Much of the early work was done by Burnett <sup>3</sup> in Australia and by Parker <sup>4</sup> in New York. Of late this exotoxin has received a great deal of attention, particularly by the English investigators. We shall not attempt to elaborate on the history of the development of the knowledge concerning the toxin.

In recovering the toxin from staphylococci it is necessary to have a dextrose-free medium and care should be taken that the  $p_H$  of the medium is adjusted and that the organism is grown under reduced oxygen tension. We shall not discuss the technical bacteriologic process by which this toxin is demonstrated but shall merely state that the toxin can be demonstrated in a filtrate so obtained which is sterile to culture both aerobically and anaerobically.

Many filtrates produce hemolysis with no necrosis, but we have not encountered a nonhemolytic filtrate which showed necrotic properties. To a degree, the power of hemolysis is an index to dermonecrosis. The necrotic property of a potent toxin frequently is found to be 7 000 dermonecrotic units per cubic centimeter of toxin. It is quite common to find a toxin which will hemolyze washed rabbit cells in a dilution of 1:1,280. Evidently this toxin has a dermonecrotic and hemolytic component in variable amounts. By injection of the toxin intravenously or intracutaneously into experimental animals, death may be produced in from a few hours to several days, depending on the amount of toxin injected and on its potency. By attaching an electrocardiograph and a pneumograph to a dog which previously had received lethal doses of staphylo toxin, Nelis and Bouckaert <sup>5</sup> showed that death was caused by ventricular fibrillation, with an attendant progressive fall in blood pressure. Animals dying after several days of toxemia show definite histologic changes, especially in the heart, kidneys and liver. That the death, necrosis and histologic changes in these cases are due to the exotoxin of the staphylococcus and not to histamine is well authenticated by the work of Dolman, <sup>6</sup> who stated "Histamine has been shown to

2 Van de Velde, H. Étude sur le mécanisme de la virulence du Staphylocoque pyazene, *Cellule* **10** 401, 1894.

3 Burnett, F. M. Exotoxins of *Staphylococcus Pyogenes Aureus*, *J. Path. & Bact.* **32** 717 (Oct.) 1929.

4 Parker, J. T. Production of Exotoxin by Certain Strains of *Staphylococcus Aureus*, *J. Exper. Med.* **40** 761 (Dec.) 1924.

5 Nelis, P., and Bouckaert, J. J. Action cardiaque de la toxine staphylococcique chez le lapin et chez le chien, *Compt. rend. Soc. de biol.* **113** 1157, 1933.

6 Dolman, C. E. Pathogenic and Antigenic Properties of *Staphylococcus Toxin*, *Canad. Pub. Health J.* **23** 125 (March) 1932.

The average duration of hospitalization was six weeks

The average period required for the sinus to close was twelve weeks

Sequestration is rare in infants. Sequestrectomy was necessary in only 6 cases. Roentgen examination frequently reveals marked destruction of the shaft with an extensive involucrum, suggesting that sequestration will occur, but this rarely happens.

If the patient survives the acute infection, the prognosis for sound bones is excellent. Recurrence almost never occurs. In only 1 of the 41 cases in which a follow-up study recently was made did examination reveal the lesion in the bone to be not clinically healed, and this was a recent case. In 1 other case the roentgenograms suggested a smoldering lesion, but there had been no symptoms since the sinus had healed.

There was residual deformity in 5 cases, mainly caused by involvement of joints.

Seventy-one patients with acute osteomyelitis were operated on. In 37 an operation on the bone was performed, usually the formation of a window, in 34 drainage of the secondary abscess or periosteal incision was performed.

The cases in the two groups showed little difference in the immediate or the final prognosis, but the comparison is inaccurate because the cases in the two groups were not comparable.

In 8 cases of acute osteomyelitis treatment was by immobilization without operation. Five patients were mildly ill, and 1, moderately ill, these 6 patients recovered completely. Two patients were critically ill, with osteomyelitis of the neck of the femur and septicemia, 1 completely recovered and the other is recovering. In none did a sinus develop.

Of the 6 patients with osteomyelitis of the neck of the femur the 3 not operated on and treated by immobilization with constant observation did better than those on whom drainage was established by surgical intervention.

It is suggested that the differences between the osteomyelitic syndrome of infants and that of older children are largely dependent on three factors. (a) The organism, *Streptococcus*, is observed more frequently in infants than in older children. (b) The anatomic construction of the bone in infants, characterized by larger cancellous spaces in the bone, allows the infection to pass more readily from its site of origin, the metaphysis to the subperiosteal space, the periosteum is more loosely attached in the infant and allows the decompression to occur, the periosteum then ruptures, allowing the pus to escape into the soft tissues, without sequestration except in rare instances. (c) The absorption of dead bone occurs more rapidly in infants as does the formation of new bone.

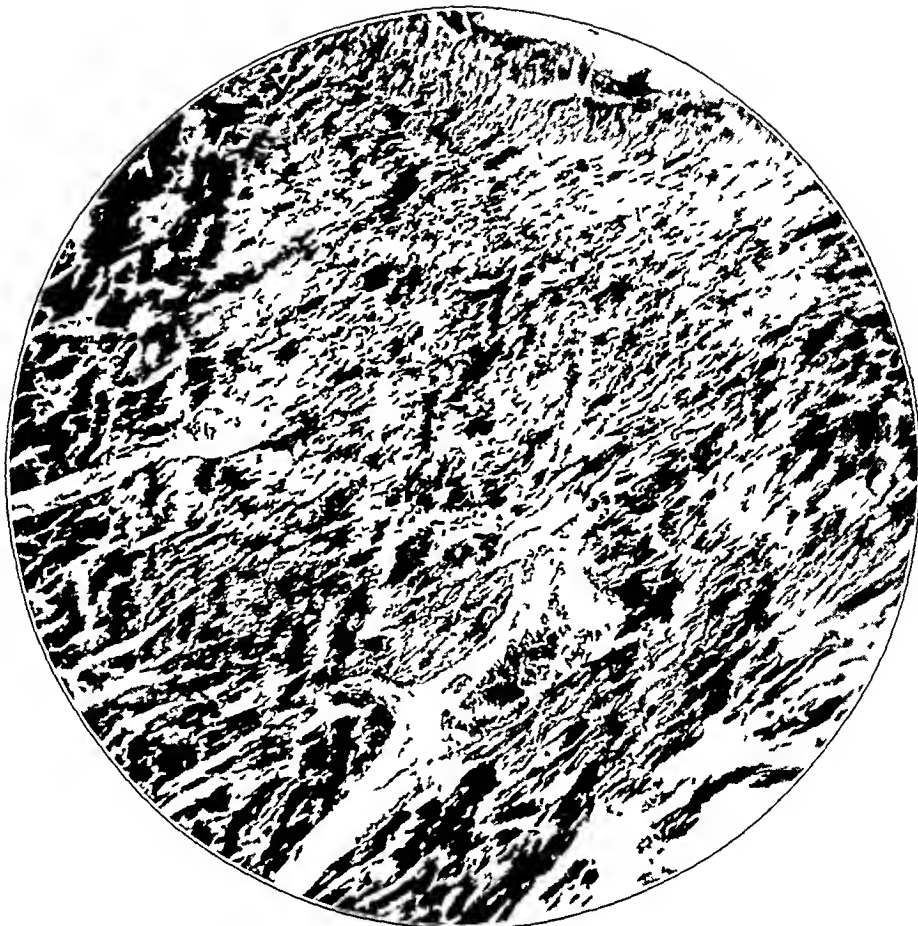


Fig 1—Low power photomicrograph of the heart of a rabbit

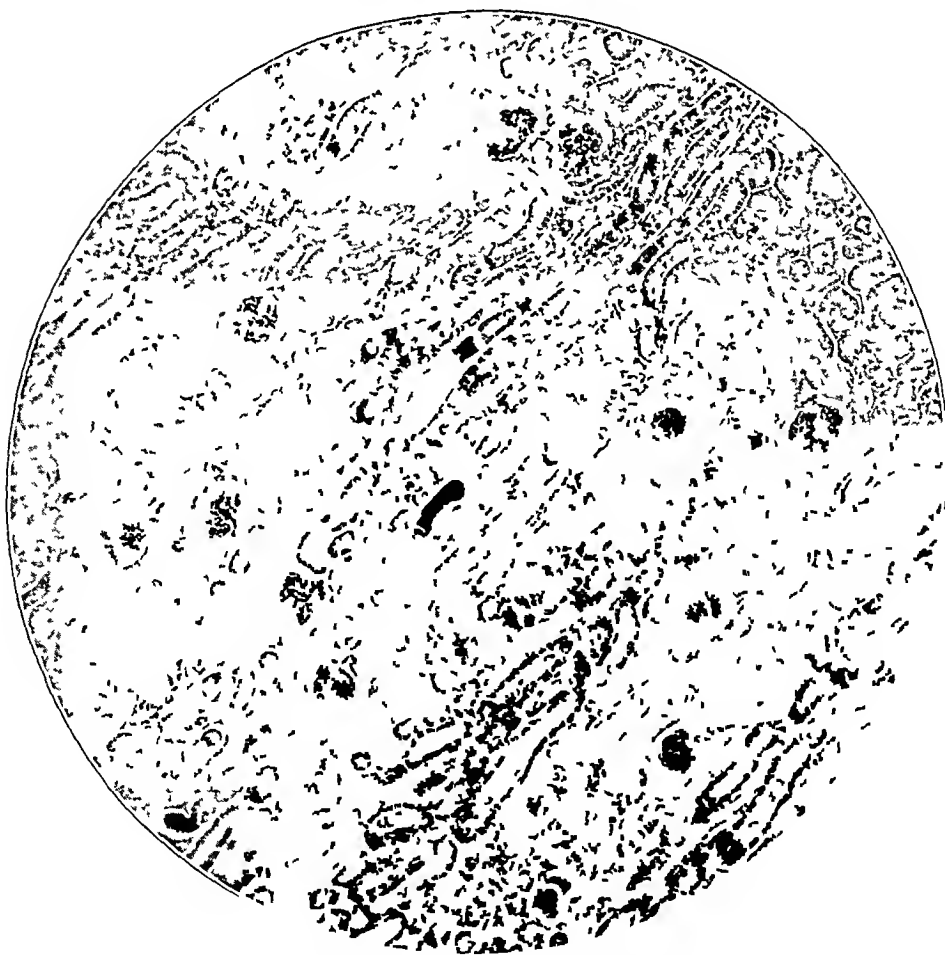


Fig 2—Low power photomicrograph of the kidney of a rabbit

disease in infants with those in older children. He mentioned the frequent incidence of septic joints and displacement of the epiphysis. He expressed the opinion that incision and drainage of the abscess are generally sufficient. The mortality rate in his series was 38 per cent.

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For statistical purposes only we have utilized the cases of 41 patients treated by the surgical service of Dr. W. S. Ladd, at the Children's Hospital.

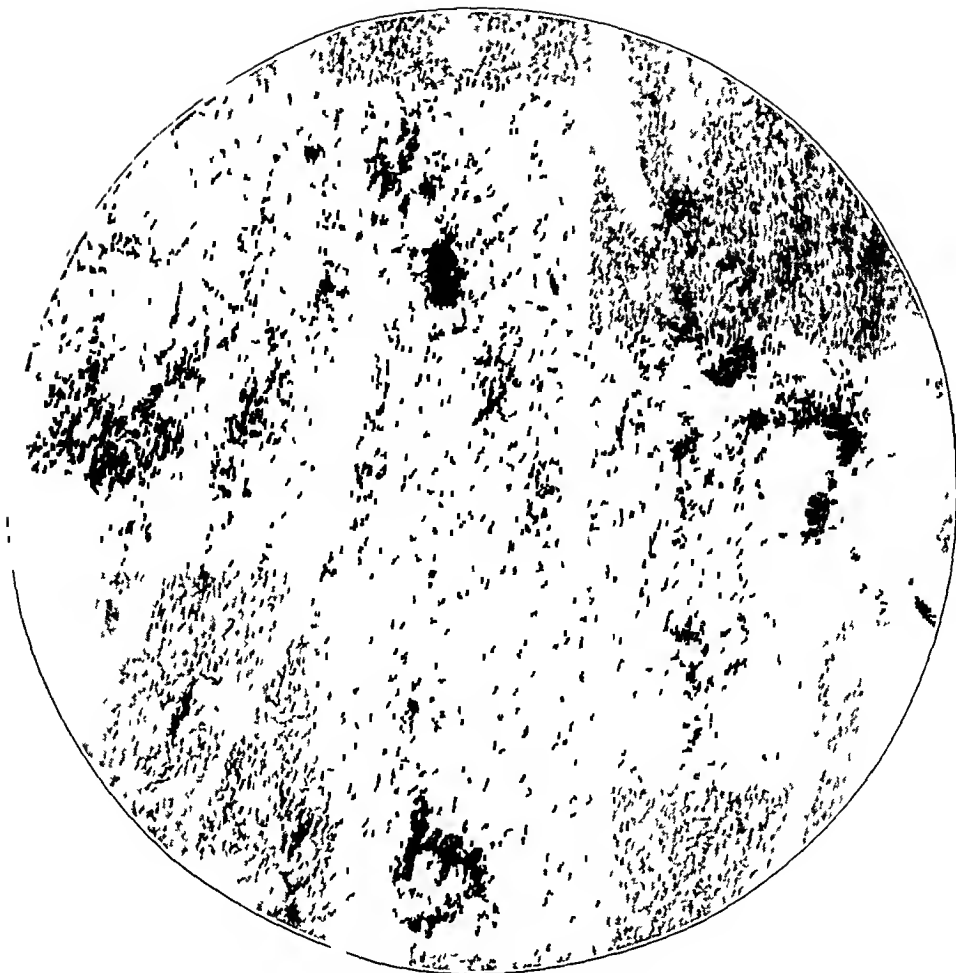


Fig 5—Low power photomicrograph of the human heart

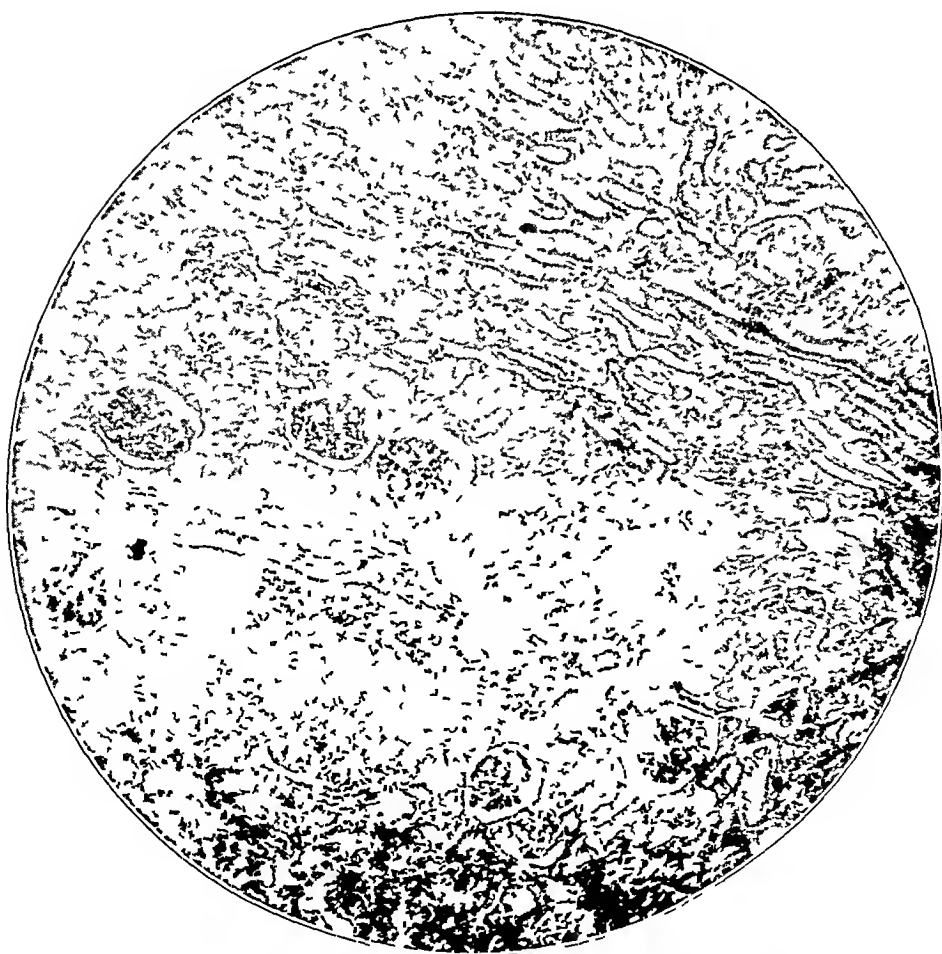


Fig 6—Low power photomicrograph of the human kidney

of the disease. This fact must be interpreted as indicating a lack of a defensive mechanism within the host, for once the host has had ample time to elaborate immune substances, the mortality drops sharply.

Most observers concede that osteomyelitis develops subsequent to some minor abrasion or staphylococcic infection occurring in the skin. Antecedent trauma is frequently an important factor in the anatomic localization of the disease. From this frequently minor port of entry in the skin the organism invades the blood stream and is hematogenically borne to the bone. When this blood-borne deposit of bacteria produces the characteristic signs of inflammation, the first localizing symptoms of osteomyelitis are manifest.

The staphylococcic flora of the normal skin is extensive. All types are found with regard to both the ability to produce pigment and the power to hemolyze blood. There is much evidence which shows that the saprophytic staphylococci of the healthy skin are capable of producing a hemolytic exotoxin, and in acute lesions of the skin this power of hemolysis is more marked. This fact in itself would indicate that on the intact skin may be found virulent staphylococci living as saprophytes, but following trauma or minor infections these potentially virulent staphylococci may become invasive and capable of producing deep lesions.

In our study of seventy-one strains of staphylococci obtained from patients with severe infections studied to date, sixty-four showed a demonstrable toxin, and in seven instances no toxin-making properties could be demonstrated. Theoretically one can postulate that invasion of the human body occurs only from potentially virulent staphylococci of the cutaneous flora.

Since furuncles are frequently a precursor of osteomyelitis, the comparative percentages in the table are of interest.

*Results of the Study of Strains of Staphylococci Obtained From Patients with Severe Infections*

Type of Infection	Total Number of Cases	Hemolysis		Necrosis		No Hemolysis		No Necrosis	
		Number of Cases	Percentage	Number of Cases	Percentage	Number of Cases	Percentage	Number of Cases	Percentage
Osteomyelitis	27	24	88.8	22	81.4	3	11.2	5	18.6
Furuncle	19	17	89.5	14	73.7	2	10.5	5	26.3
Pyemia	4	4	100	4	100				
	3	2	66.6	2	66.6	1	33.3	1	33.3
Cavernous sinus thrombosis	4	4	100	3	75			1	25
	4	4	100	4	100				
	5	4	80	3	60	1	20	2	40
	1	1	100	1	100				
	1	1	100	1	100				
Cellulitis	3	3	100	3	100				
Totals	71	64	90.1	57	80.5	7	10.5	14	19.5
Average	5					5		5	

toxin makers. These organisms were obtained from persons with acute hematogenous osteomyelitis or with an acute recurrence at the time of operative procedure. No culture was utilized from draining sinuses.

From experiments in immunization conducted on rabbits and other experimental animals with the staphylococcus toxin, it was found that the laboratory animal requires approximately two weeks to make an immune response to the free staphylococcus toxin used as an antigen. Also, from the fact that antitoxic substances against the free toxin of the staphylococcus have been shown to be consistently present in the human blood serum by Neisser and Wechsberg,<sup>7</sup> and lately emphasized by Parish, O'Meara and Clark,<sup>8</sup> one must assume that staphylococcus antitoxin is one of the defenses of the body against the invasion of toxigenic staphylococci. Clinically this is supported by the observation that in osteomyelitis the blood stream sterilizes itself at approximately the time required for the human organism to respond to the staphylococcal antigen. One must remember that over 90 per cent of the deaths that occur from acute staphylococcal osteomyelitis take place within the first two weeks of the disease, before the body has had ample opportunity to elaborate antitoxic substances. These clinical observations support the laboratory observations that the antitoxin in the blood is of importance in the defense against these toxigenic staphylococci.

It is not uncommon to find that the most virulent toxin-making staphylococci may be isolated from a person with osteomyelitis of minor clinical severity. This is evidence that the defenses of the body are able to cope with this infection, and one finds a high titer of antitoxin in the blood taken from these patients. Conversely, severe osteomyelitis may be present in a person who shows little antitoxic titer in his blood. Staphylococci isolated from such patients may show but a slight degree of toxin-making property although the clinical symptoms may be alarming.

The beneficial results obtained in the treatment of acute osteomyelitis by transfusion of blood from an adult donor may be due in part to the titer of staphylococcus antitoxin consistently present in the blood serum of the adult.

Lately Parish and his collaborators determined methods for the measurement of the antitoxin content of the blood. Unfortunately at the present time there is no generally accepted standard of procedure, and each worker utilizes a different standard of measurement, the results therefore necessarily become comparative.

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<sup>7</sup> Neisser, M., and Wechsberg, F. Ueber das Staphylococcin, *Ztschr. f. Hyg. u. Infektionskr.* **36** 299, 1901.

<sup>8</sup> Parish, H. J., O'Meara, R. A. Q., and Clark, Winnifred H. M. Clinical Investigation of Staphylococcal Toxin, Toxoid and Antitoxin, *Lancet* **1** 1054 (May 19) 1934.

be present in the original broth. Such amounts of histamine could not possibly be responsible for any of the characteristic features of the toxin. Moreover, if the histamine content of the toxin be destroyed by incubating it with histaminase the original properties of the toxin remain unimpaired. Moreover this toxin forms a toxoid when treated with formaldehyde.

It has long been suspected that in osteomyelitis a free toxin is present and that many of the symptoms are attributable to an existing toxemia. Postmortem examination of patients dying within the first two weeks of the disease shows histologic changes pointing to a condition of extreme toxemia. These findings are not unlike those in the rabbit subjected to lethal doses of staphylococcal toxin as evidenced by the following histopathologic report:

The section of cardiac muscle of a rabbit depicted in figure 1 shows alternate dark-staining muscle fibers and light-staining muscle fibers. The light-staining fibers show considerable longitudinal fibrillation. The darker muscle fibers show peculiar obliteration of the striations, with no perivascular infiltration about the blood vessels. The microscopic diagnosis was toxic myocardial degeneration.

The section of the kidney of a rabbit shown in figure 2 reveals considerable exudate in the capsule of Bowman marked by light-staining coagulated protein with compression of the capillary tufts. The proximal convoluted tubules show marked cloudy swelling and more or less desquamation of the tubular epithelium. The passive congestion is more or less marked. All tubular structures show evidence of a varying degree of cloudy swelling. There are no interstitial changes and no marked round cell infiltration. The microscopic diagnosis was acute parenchymatous degeneration with glomerular exudate.

The outstanding feature in the liver of a rabbit a section of which is shown in figures 3 and 4 is a large thrombus in the branch of the portal vein. In the immediate environ of this thrombus is a large area of necrosis, demarked sharply from living liver cells. The liver cells in the viable area are well stained and show no marked deviation from the normal. In some of the portal canals round cell infiltration is marked. The blood vessels show marked passive congestion of the liver columns. In general they are arranged well and not broken up by central necrosis. The microscopic diagnosis was thrombotic necrosis of the liver with round cell infiltration.

The muscle fibers of the human heart shown in figure 5, are of small diameter and are richly nucleated. The blood vessels are widely dilated. A high power view reveals poorly developed cross-striation of fibers, which take a deep eosin stain and show considerable cloudy swelling. There are no other material changes. Here and there are small foci of round cell infiltration of muscle fibers and extravasation of blood into the fibers. The microscopic diagnosis was acute congestion of the muscle of the heart with evidence of infective inflammation.

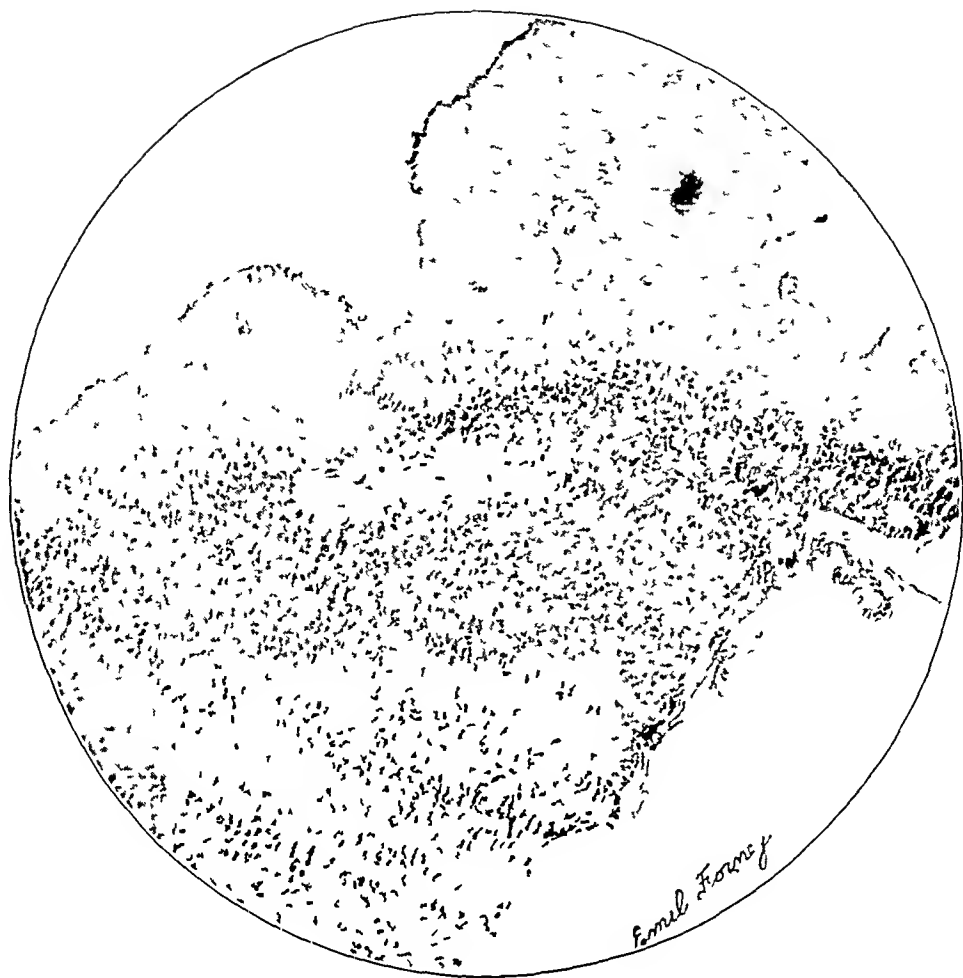
Figure 6 shows much necrotic coagulation in the tubules of this human kidney. Marked passive congestion is present everywhere. The glomeruli are swollen generally occupying the capsules of Bowman tightly. The passive congestion in many parts has proceeded to the passage of blood in the tubular structures. All the tubules are involved in a necrotic process. There is cast formation in the tubules.



antitoxin in an attempt to procure passive immunization. The fact that the immune titer of antitoxin is infinitely higher than that of ordinary adult blood used in transfusion in an effort to combat toxemia and destruction of blood should indicate that this procedure is worthy of serious consideration. Pronounced early anemia, so frequently observed, is strong presumptive evidence that the invading organism is toxigenic with marked properties of hemolysis. That the natural antitoxin does not appear in great quantities until after the second week of the infection, together with the fact that the majority of deaths from osteomyelitis occur within the first two weeks of the disease, indicates that the optimum time for antitoxin therapy is early in the course of the infection. This contention is supported by the fact, as previously mentioned, that material obtained post mortem from patients dying early in the course of the disease and from rabbits dying from lethal doses of toxin shows marked toxic degeneration, particularly in the heart, kidney and liver. Once the blood stream has become sterile, with the process localized in the bone, and the body defenses have reacted to the antigen, there is, in our judgment, little to be hoped for from the administration of antitoxin. In the light of the present knowledge, we can only say that staphylococcus antitoxin will neutralize the free toxin fraction. We have on repeated occasions actively immunized rabbits, by the use of staphylo toxin, against several times the lethal dose of toxin. Animals inoculated with virulent living staphylococci live longer when antitoxin is administered. In a series of rabbits receiving living staphylococci one half of those which were treated with staphylococcus antitoxin showed a slightly lower mortality than the controls which received no antitoxin.

The possibility of active immunization has received some attention, since the fact has become known that staphylococcus toxin which has been treated with formaldehyde and incubated at 37 C. for a period of days forms toxoid which has antigenic properties. The advisability of using vaccines in an attempt to create active immunity is not attended with unanimity of opinion. Our experience in conjunction with a study of the available reports in the literature indicates that unquestionably the use of staphylococcus toxoid raises the immune titer in man as well as in laboratory animals.

The problem of recurrence in osteomyelitis is yet to be elucidated. It is possible that recurrences may be associated with a fall in the immune titer of the blood, which is familiarly spoken of as lowered resistance. At the present time all our attempts to measure the titer of immune substances in chronic osteomyelitis have shown a high degree of protective substances. It is our opinion that the defensive substances of the blood measured over a long period of time may disclose valuable information relative to the relapse in the patient who has had osteomyelitis.



Figs 3 and 4—Low power photomicrographs of the liver of a rabbit

# A HISTOLOGIC STUDY OF MECKEL'S DIVERTICULUM

## WITH SPECIAL REFERENCE TO HETEROTOPIC TISSUES

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The recent literature contains numerous references to gastric mucosa adjacent to the so-called "peptic ulcers of Meckel's diverticulum." In these articles interest is almost entirely restricted to the clinical aspects of the anomaly. My purpose in this paper is to report the histologic observations in nineteen new cases of Meckel's diverticulum and to collect the previous data on the incidence, position and types.

The first case of Meckel's diverticulum mentioned in the literature is that of J. H. Lavater in 1672. In 1698 Ruysch referred to this diverticulum, and in 1701 he published an illustration of an additional case. Littre in 1742 observed such a diverticulum in a hernia. However, until the time of Meckel little was known of the diverticulum which bears his name. In 1808 he mentioned it, and in 1812 he wrote the first accurate description of the diverticulum, giving its embryologic background and emphasizing its clinical importance. In this connection it is interesting to note that as far back as 1769 Morgagni stated that he had observed in several instances a diverticulum on the intestine of a goose.

### MATERIALS

The material used in this investigation consisted of nineteen diverticula, ten of which were supplied by Dr. J. S. Horsley of St. Elizabeth's Hospital, Richmond, Va. Five operative specimens and three autopsy specimens came from the Laboratory of Pathology of the University of Virginia Hospital. Nine of the specimens (cases 1 to 9) from Dr. Horsley were of the usual type with a lining of mucosa typical of that seen in the small intestine, with numerous cells of Paneth. The specimen in case 10 was unusual in that it had numerous protrusions. The five operative specimens from the University of Virginia Hospital included two with an area of gastric mucosa, the three autopsy specimens included one with such an area. The nineteenth specimen came from Dr. T. P. Bagwell of Grace Hospital, Welch, W. Va. This specimen was ulcerated and contained a patch of gastric mucosa.

Except where otherwise indicated, slides were made from the tip of the diverticulum, because without exception when the position of the heterotopic tissue was noted in the literature it was always found in the

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From the Laboratory of Histology and Embryology, University of Virginia

in fair abundance. The microscopic diagnosis was extreme renal congestion with necrosis of the tubular epithelium most marked in the proximal convoluted tubules.

The human liver depicted in figure 7 shows an advanced degree of passive congestion. The columns of liver cells are reduced in breadth by congestion of the blood vessels of the sinusoids of the liver. A few spots show the beginning of fibrous tissue formation. The portal canals show marked round cell infiltration. The Kupffer cells are increased in number and contain hemosiderin pigment. The microscopic diagnosis was subacute hepatitis with marked congestion and round cell infiltration.

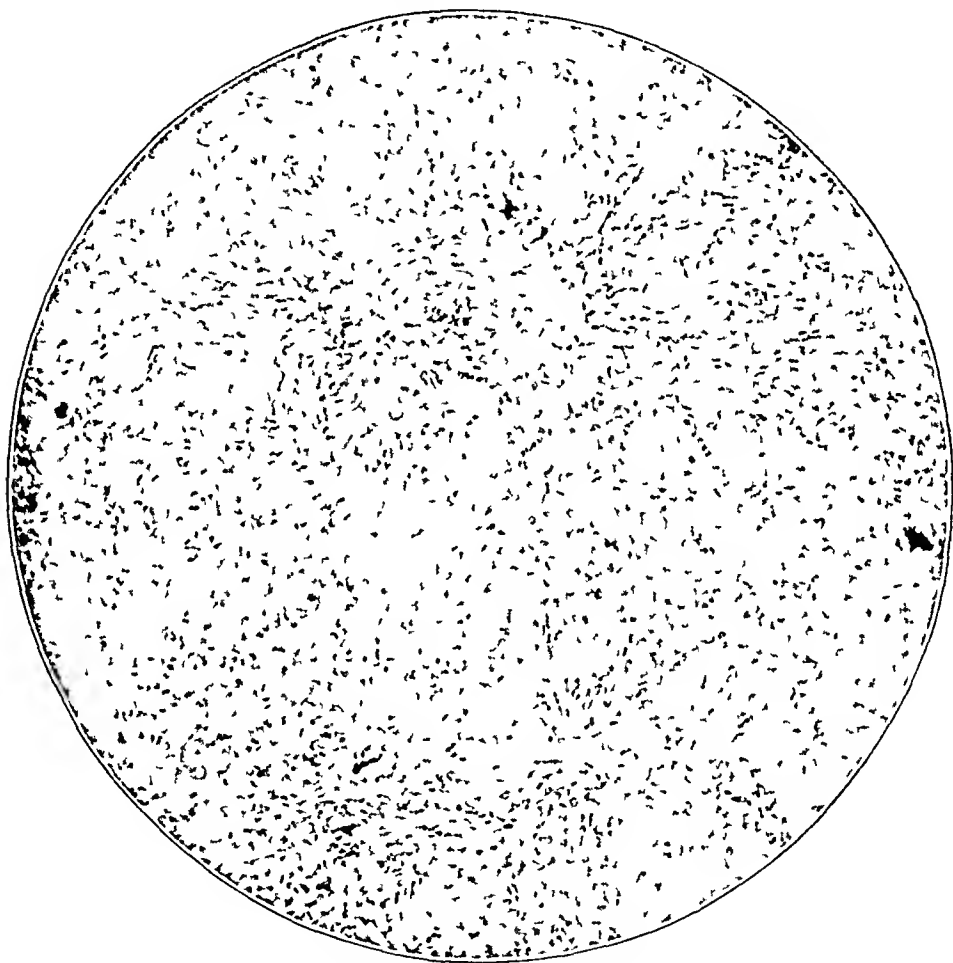


Fig 7—Low power photomicrograph of the human liver

We have to date studied the toxin-forming properties of twenty-seven strains of staphylococci obtained from cases of osteomyelitis. It is interesting to note that in twenty-nine cases of osteomyelitis the staphylococcus was isolated twenty-seven times. Of the twenty-seven cultures, twenty-four were hemolytic, twenty-two necrotic, three non-hemolytic and five non-necrotic. If one considers hemolysis as evidence of the formation of toxin, this would mean that in twenty-seven cases of staphylococcic osteomyelitis twenty-four of the invading organisms were

cells clearly visible. In other areas the glands beneath this epithelium seem less differentiated, and parietal cells could not be made out. Such areas were presumably pyloric. In many areas intestinal and gastric glands were mixed. Eosinophils were especially numerous throughout the mucosa of the diverticulum.

CASE 13—The specimen was obtained at autopsy from Miss M. P., aged 23, and was supplied by the department of pathology of the University of Virginia. It measured 6 by 2.5 by 2 cm. Microscopic study revealed typical intestinal mucosa. The cells of Paneth were especially prominent, frequently lining the entire tip of the fundus of the intestinal glands.

CASE 14—The specimen was obtained at operation and was supplied by the department of pathology of the University of Virginia. Its dimensions were 3.5 by 2 by 1.5 cm. Microscopically, a subacute inflammatory condition was found. There was a purulent exudate in the lumen, and the mucous membrane was infiltrated with polymorphonuclears and lymphocytes. Most of the diverticulum was lined with mucosa like that seen in the small intestine. An area about 1 cm. in diameter had clear, faintly pink-staining columnar cells. Under these there was marked infiltration, but in a few areas parietal cells could be identified.

CASE 15—The specimen was obtained at autopsy and was supplied by the department of pathology of the University of Virginia. Microscopic study disclosed mucosa like that seen in the small intestine and many cells of Paneth in the base of the intestinal glands.

CASE 16—The specimen was obtained at operation and was supplied by the department of pathology of the University of Virginia. Gross examination revealed marked inflammation and ulceration. On microscopic examination an inflamed and eroded mucous membrane of the type seen in the small intestine was found, with a small number of the cells of Paneth present in the bases of some of the intestinal glands.

CASE 17—The specimen was removed at operation from Mr. C. F., and was obtained from the department of pathology of the University of Virginia. Gross examination disclosed that the diverticulum measured 3.8 by 2.1 by 2.6 cm. and that the mucosa of the tip appeared swollen.

Microscopic examination revealed gastric mucosa of the fundic type throughout most of the diverticulum. This consisted of tall, clear, pink-staining columnar cells lining the ducts of the gastric glands. The fundus of the glands was quite long, and typical chief and parietal cells were found. The muscularis mucosae was doubled in the gastric portion, and in one area under the gastric mucosa the muscularis consisted of three layers. An area of pyloric mucosa was found. In this area the parietal cells were few and scattered, and the gastric crypts were deep. In one portion of the submucosa there was a mass of pancreatic tissue 8 mm. in diameter. There were well developed ducts, and although islets were present they were difficult to find.

CASE 18—The specimen was removed from Miss M. H. P. at the time of operation for salpingectomy. It was obtained from the department of pathology of the University of Virginia. The mucosa was of the type characteristic of the ileum (fig. 1).

CASE 19—The specimen was removed from a young man by Dr. T. P. Bagwell at Grace Hospital, Welch, W. Va. Preoperatively, the condition was diagnosed as a perforated duodenal ulcer, but at operation a perforated Meckel's diverticulum was found. After preservation in 95 per cent alcohol, the specimen measured 4.5 by 30 mm. A small clearcut ulcer 5 mm. in diameter could be seen

In the study of the blood of one hundred persons of unknown history in our laboratory, the staphylococcus antitoxin titer was measured and found to average 1:16. In the measurement of the antitoxin of persons suffering from chronic osteomyelitis, the titer was found to be as high as 1:4000 but the average was found to be many times the normal. The following tabulation shows the antihemolytic titer of normal persons and of those with osteomyelitis (the asterisk indicates recurrence of osteomyelitis one week after the measurement of the titer).

Dilution	No.	1:4	1:8	1:16	1:2	1:6	1:12	1:24	1:48	1:96	1:192	1:384	1:768	1:1536
Blood of normal persons	100	21	1	0	1*	4	1	0	0	0	0	0	0	0
Blood of persons with osteomyelitis	%	0	0	1	6	5	0	2	4	4	4	4	2	2

The technique of the measurement of the antitoxin content of the blood as developed by Parish is based on the ability of the free antitoxin of the blood serum to be bound to a known quantity of staphylo toxin, a suspension of washed rabbit cells being used as an indicator. If the toxin is in excess, hemolysis will take place. The end-point is margined sharply.

Commercial staphylococcus antitoxin now available for experimental use according to our method of measurement shows an antihemolytic titer approximately 700 times that of ordinary blood serum. Commercial manufacturers standardize antitoxin by its power to neutralize a definite number of dermonecrotic doses of toxin per cubic centimeter of antitoxin. A potent staphylococcus toxin will measure about 5,000 to 7,000 dermonecrotic doses per cubic centimeter. The rabbit, because of its low natural antitoxin titer is the animal of choice for this measurement. The standard antitoxin will neutralize 100,000 dermonecrotic doses of toxin per cubic centimeter. This antitoxin is the concentrated pseudoglobulin fraction of horse serum in which fraction the immune substances are carried.

In a study of the immunology of osteomyelitis several factors present themselves. We found in a summary of three hundred cases of osteomyelitis that the youngest patient encountered was 3 months of age, the average age being 13 years. The low age incidence of this disease suggests an accidental factor coupled with a low incidence of immunity in childhood against virulent staphylococci which are commonly present on the normal healthy skin as saprophytes. Evidence is rapidly accumulating that the titer of natural antitoxin present in the blood plays an important part in the protection of the host against this infection.

The high titer of available staphylococcus antitoxin immediately suggests the possibility of therapeutic attainments by the use of this



Fig 3 (case 19) —Portion of a fundic gland from figure 2, showing the parietal cells ( $\times 1,000$ )



Fig 4 (case 19) —Vertical section of the mucosa of Meckel's diverticulum adjacent to the area of figure 2, showing long intestinal glands similar to those of the colon except for fewer goblet cells. Between these two areas occurs a narrow region with short stout villi and long intestinal glands with many goblet cells ( $\times 96$ )

The therapeutic use of staphylococcus antitoxin in acute osteomyelitis and attempts to vaccinate the patient with chronic osteomyelitis by the use of toxoid will be the basis of further reports.

#### CONCLUSIONS

Of 27 cases of osteomyelitis of staphylococcic etiology, a free toxin was demonstrated in 88.8 per cent.

Of 44 cases of deep staphylococcic lesions exclusive of osteomyelitis, a free toxin was demonstrated in 91 per cent.

There is a resident titer of antitoxin against staphylococcus toxin in normal adult blood serum.

In chronic osteomyelitis this immune titer is markedly increased.

In the treatment of acute staphylococcic osteomyelitis a donor known to have a high antitoxic titer should be procured.

Dr. Ralph Emerson Duncan printed the cooperation of the laboratory and the use of its facilities and Dr. Frank T. Hall interpreted the pathologic and histologic specimens. The Lederle Laboratories supplied the antitoxin and some of the cultures.



Serial sections were made of the area about the ulcer. The rest of the diverticulum was cut into sixteen pieces, and slides were made from each piece.

Microscopically, the ulcer appeared to be subacute. The peritoneal surface about the ulcer showed a marked inflammatory reaction with a thick layer of leukocytes and fibrin and an attempt at organization of the exudate. The ulcer was surrounded by intestinal mucosa. An area about 16 mm from the ulcer (as measured by serial sections) showed gastric mucosa typical of that seen in the fundus. On microscopic examination of the slides of the rest of the diverticulum it was noted that the distal fourth of it was lined with gastric mucosa (fig 2). The gastric mucosa was from four to five times as thick as the intestinal mucosa of the proximal part. The fundus of the glands was from six to seven times as long as the ducts. In the fundus typical chief and parietal cells were found. The parietal cells were quite numerous (fig 3). The ducts were lined with tall, columnar, clear, faintly pink-staining cells. No Paneth cells were found in any of the sections which revealed intestinal mucosa. A small area of the mucosa surrounded by typical intestinal mucosa with villi had the appearance of the mucosa of the colon (fig 4).

TABLE 2—*Data in Additional Cases of Umbilical Polyps and Fistulas with Gastric Mucosa, Compiled from the Literature*

Date	Author	Sex of Patient	Type of Mucosa
1850	Gould	? (not recorded)	? (not recorded)
1881	Tillmans	?	?
1887	Roser	M	?
1888	van Heukelom	?	Pyloric
1889	von Rosthorn	?	Pyloric
1898	Reichard	?	?
	Weber	?	Pyloric
	Lindner	?	Pyloric
1899	Lever	?	Pyloric
1903	Strada	?	Pyloric
1904	Salzer	?	Cardiac
1905	Minelli	?	Gastric adenoma
1908	Denuece	?	Fundic
1911	Negroni	?	?
1922	Nicholson	?	?
1923	Stone, Eric	?	?
	Nicholson	?	Fundic and pyloric
1925	Taylor	?	Fundic
1931	Lindau and Wulff	?	?
1933	Hudson and Koplik	?	?

#### CASES REPORTED IN THE LITERATURE

Data in cases of Meckel's diverticulum with gastric mucosa, compiled from the literature, are presented in table 1.

Hilgenreimer, while not stating that his specimen contained gastric mucosa, published an illustration of a diverticulum in which the distal end had a much thickened mucosa which was probably gastric in nature.

Since umbilical polyps and fistulas are also remnants of the vitelline duct, a list of the cases of these conditions with gastric mucosa is included (table 2).

Kustner described some columnar cells which he thought came from the urachus in an umbilical adenoma. From the illustration they look somewhat like gastric glands.

apex. In the case of an unusual diverticulum, slides were made from all parts. All the specimens were stained with hematoxylin and eosin as a routine measure and all were embedded in paraffin and cut into sections at intervals of 7 or 10 microns.

CASES 1 to 9—The diverticula in this group were of the usual type with mucosa like that of the ileum. The specimens need not be described further.

CASE 10—The diverticulum was supplied by Dr. Horsley. It was a sausage-shaped mass 17 by 10 mm. From various parts of its surface projected seven protrusions which varied in size and were irregularly placed. The diverticulum was connected to the ileum by a very small stalk. Approximately eighty slides were made of this diverticulum, and the sections were so spaced as to show parts from the whole specimen.

Microscopically, the specimen was found to contain typical intestinal mucosa with very distinct goblet cells and villi. The protrusions were plainly seen in certain of the sections. They consisted of a lining epithelium, which was continuous with that of the diverticulum and an outer lamina muscularis mucosae. In one section especially it was very easy to see that the epithelium, the lamina muscularis mucosae and the lamina propria of the protrusion were continuous with that of the diverticulum. Outside of the mucous membrane of the protrusion was a layer of areolar tissue which contained numerous blood vessels. This seemed to be continuous with both the submucosa and the fibrous coat of the diverticulum. The muscular coat stopped short at the lateral border of each protrusion, so that the delicate lamina muscularis mucosae constituted all the muscular tissue found in the protrusion. Neither the diverticulum nor any of its protrusions were inflamed. Moderate numbers of Paneth cells were present.

CASE 11—The specimen was obtained at autopsy on a young man and was supplied by the department of pathology of the University of Virginia. The diverticulum was situated 100 cm. from the ileocecal valve. Macroscopically it was a pouch, wider at the neck than at the tip and measured 55 by 25 mm. No gross lesions were visible. Microscopic study was based on sections taken from seven regions. In the tip of the diverticulum an area estimated to be from 3 to 4 mm. in diameter was found to contain gastric mucosa. The gastric mucosa was from two to three times as thick as the intestinal mucosa. It contained tall, clear pink-staining columnar cells. In the tunica propria could be seen the fundic glands, with both chief and parietal cells visible. However the parietal cells were not especially numerous. Paneth cells were numerous in the fundus of the glands of the intestinal mucosa.

CASE 12—The specimen was removed by Dr. Bruce Morton in the course of an appendectomy on Mr. K. B. The gross pathologic report from the pathologic department stated: "The specimen was 5 cm. in length, consisting of a pouch, the open end of which was intestinal wall. The distal end was bulbous and irregular and somewhat firmer. In cut section the mucosa appeared normal. In the distal end the mucosa was piled up to entirely fill the lumen." The bulbous mass at the distal end was 15 mm. long, and there was some ulceration and inflammation.

As seen in microscopic sections, the mucosa of the distal end was very thick and thrown into folds. The lining epithelium of these folds was made up of tall columnar cells which stained faintly pink. In certain areas beneath these columnar cells could be seen typical fundic glands, with the chief and parietal

the digestive tract from the pharynx to the rectum and all the glands associated with this tract, with the possible exception of the parotid gland. In Meckel's diverticulum alone almost all of the differential potentialities of this endoderm may be realized.

TABLE 3—*Reports of Duodenal Glands in Additional Data on Meckel's Diverticulum*

Date	Author	Additional Data
1897	Kern	
1906	Hedinger	Pancreatic tissue also
1909	Tschiknawerow	
1912	Koch	
1925	Schaetz	Male, gastric mucosa also
1930	Teyre, Patel and Lepart	Male
1932	Hudson and Koplik	
	McCann	Male, pancreatic tissue also
1933	C. W. Mayo	Gastric mucosa also
1934	Schullinger and Stout	Gastric mucosa also

TABLE 4—*Reports of Pancreatic Tissue in Meckel's Diverticulum*

Date	Author	Additional Data
1861	Zenker	
1870	Neumann	
1891	Schmauser	
1893	Schirmer	
1899	Brunner	
1901	Wright	Islets
	E. Albrecht	Islets
1904	Bize	
1905	Merkel	
	Deye	
1906	Hedinger	Duodenal mucosa also
1907	Deetz	Male, gastric mucosa also
1908	Ologg	
	Kothe	Man
1909	Nazari	
	Busch	
1910	Albrecht and Arzt	
1911	Tschiknawerow	
1912	Koch	Two cases with gastric mucosa also
	Drummond	Female
	Sil	
1916	Cullen	
1922	Cullen	
1925	Schaetz	Male, islets present
	Schaetz	Female islets and gastric mucosa
	Schaetz	Male, fundic, pyloric and cardiac glands also
	Steiger	
1927	J. B. Stone	
	Taylor	Three cases all with gastric mucosa and islets
	Winkelbauer	Male, gastric mucosa also
1928	Cogniaux	
1932	Hudson and Koplik	
	Mason and Graham	Male, gastric mucosa also
	McCann	Islets and duodenal glands
1934	Hunt and Bonesteel	Male, gastric mucosa and islets

The investigators listed in table 3 have reported duodenal glands in cases of Meckel's diverticulum.

Investigators who have found pancreatic tissue in cases of Meckel's diverticulum are listed in table 4.

The type of mucosa characteristic of the colon has been reported in Meckel's diverticulum by Hudson and Koplik (two cases) and by Stern



Fig 1 (case 18)—Transverse section of the wall of Meckel's diverticulum showing tall typical villi and short intestinal glands ( $\times 96$ )

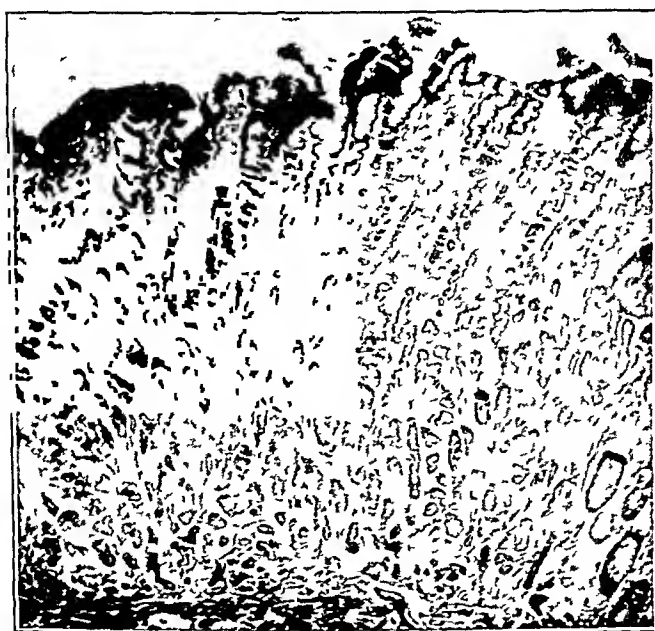


Fig 2 (case 19)—Vertical section of the gastric mucosa of the apical portion of Meckel's diverticulum, showing typical fundic glands ( $\times 96$ )

glands of the gastric type, three cases of tuberculous ulceration of the intestines which showed gastric glands in the area about the ulcer and one case of a pancreatic cyst which was in part lined by gastric mucosa Poncher and Milles found two tumors in the mediastinum of an infant These tumors were presumably of enterogenous origin, and in the case of each there was noted a small area of gastric mucosa In this same infant the small intestine was reduplicated in the lower part The reduplication opened into the intestine 20 cm above the ileocecal valve but ended blindly This blind end was found to be lined with gastric mucosa of the fundic type

The actual autopsy reports do not bear out the figures usually given for the occurrence of Meckel's diverticulum Table 5 contains a list of reports collected from the literature on this subject It is really a

TABLE 5—*Incidence of Meckel's Diverticulum as Found in the Literature*

Source of Data	Number of Cases of Meckel's Diverticulum	Number of Autopsies
Kelynaeh	18	1,446
Schmidt	14	1,822
Mitchell	39	1,635
Hilgenreiner	33	1,767
Augler	4	200
Augler	1	100
Testat, 1888	16	769
Testat, 1892	4	293
Rogie	8	400
Boston City Hospital	11	1,882
Johns Hopkins Hospital	15	2,600
Dresden City Hospital	8	8,133
Anatomic Society of Great Britain and Ireland	16	769
Bender Hygiene Laboratory	5	953
Turner	81	10,860
Sandlos	14	1,300
Baby Hospital	63	5,768
Schaetz	17	737
Total	367	40,439

collection of several series of statistics, and in only a few cases was the original article available All the available figures on the subject have been included in order to get a large enough number to give an adequate basis for reliable estimation

The average incidence in this table is about 0.9 per cent Figures given by other writers are Adam, 2.7 per cent, Fuchsig, 2 per cent, Coleman, 1.8 per cent, Harbin, 2 per cent, and Abt and Strauss, from 1 to 3 per cent

The statement usually made with reference to the sex incidence of Meckel's diverticulum is that it occurs three times as often in the male as in the female It is of interest to note that eight of the ten specimens submitted by Dr Horsley were from females and none contained gastric mucosa An average of all the figures that could be collected on the subject seem to bear this out (table 6)

TABLE 1—Data in Cases of Meckel's Diverticulum With Gastric Mucosa,  
Compiled From the Literature\*

Date	Author	Sex of Patient	Type of Mucosa
1903	Hilgenreimer	M	? (not recorded)
1904	Koch	? (not recorded)	Fundic
1906	Hildebrandt	F	?
	Koch	?	Pyloric
1907	Deetz	M	?
1909	Kohlmeier	?	?
	Koch	?	Pyloric
1912	Koch	?	Pyloric
	Koch	?	Fundic
	Koch	?	Fundic
1913	Hubschmann	M	Fundic
1915	Callender	?	Fundic
	Gramen	M	Fundic
1918	Meulengracht	M	Fundic
1919	Goetsch	M	Fundic
	Müller	M	Fundic and pyloric
1920	Barron	M	Fundic
1922	Vege and Dunant	M	Fundic and pyloric
1923	Schaez	M	Fundic and pyloric
	Schaez	M	?
	Stone, Eric	M	Fundic
	Nicholson	M	Fundic
1924	Hallopeau and Humbert	M	?
	Guibal	M	Fundic
	Brasser	M	Fundic
1925	Schaez	M	Pyloric
	Schaez	M	?
	Schaez	F	?
	Schaez	M	?
	Schaez	F	?
	Schaez	M	Fundic, pyloric and cardiac
	Pascal	F	?
	Ulrich	M	?
1926	"	?	?
	"	M	Fundic
1927	Abt and Strauss	?	?
	"	F	?
	"	M	Fundic
	"	M	Fundic
	"	M	Fundic
	Taylor	M	Fundic
	Taylor	M	Fundic and cardiac
	Taylor	M	Fundic
	Taylor	M	Fundic
	Taylor	F	Fundic
	"	M	?
	"	F	?
	"	?	?
1928	"	F	Fundic
	"	M	Fundic and pyloric
	Peterman and Seeger	M	Fundic
1929	Franko	?	?
	Winkelbauer	M	?
	Winkelbauer	M	?
	Treplin	?	?
1930	von "	M	Fundic
	von "	F	Fundic and pyloric
	Asch	M	Fundic
	Asch and Kautz	F	?
	Febre, Patel and Lepart	M	?
	Green	M	Pyloric
	Schmidt	M	?
	Edwards	M	Fundic
1931	Lindau and Wulff	M	Fundic
	Greenwald and Steiner	M	?
	"	F	Fundic
	"	?	?
	Cobb	M	Fundic
1932	Debre, Bopp and Semelaigne	M	?
	Roudil and Marty	F	?
	Singer and Vaughan	M	?
	Royter, H. A.	?	?
	Wason and Graham	M	Fundic
	Hudson and Koplik	?	? (9 cases)
	Hudson	?	Fundic (2 cases)
	Hudson	?	Pyloric
	de Vernejoul	M	?
	Schraff	M	Fundic
1933	Smith and Cohen	M	?
	Hudson and Koplik	?	? (6 cases)
	Draistedt	?	Fundic
	Mayo, C. W.	M	?
	Miller and Wallace	?	?
	Clark, D. J.	M	Fundic
1934	Boch, H.	M	?
	Hunt and Bonesteel	M	Fundic
	Schullinger and Stout	M	?

\* References to the cases cited in this and in the following tables are to be found in the bibliography.

stomach was severed by the primitive rotation of the stomach. Weber, Reichard and Roser accepted this view.

Van Heukelom in 1888, after examining a series of embryos, expressed himself as being unable to understand how a diverticulum from the stomach could possibly get to the umbilicus in view of the fact that a large liver is between the stomach and the umbilicus at the stage when the vitelline duct is supposed to atrophy (7 mm stage, 38 days). In one of his fetuses he found an area of gastric mucosa connected with Meckel's diverticulum but not in communication with its lumen. Because of this lack of communication, he postulated that there was a substance in the intestines which stimulated the intestines to form intestinal mucosa and the lack of which was necessary to the formation of gastric mucosa. He assumed that this substance was bile. This view has recently been supported by the discovery of a similarly placed area of gastric mucosa in a strand of tissue between the ileum and the umbilicus by Barron. However, so many cases of gastric mucosa in Meckel's diverticulum in free communication with the lumen of the ileum have been found that the theory of van Heukelom cannot in its entirety be true.

Salzer in 1904 proposed the theory that irritation and inflammation stimulated the endoderm to grow in a manner foreign to that particular region. There is perhaps an element of truth in his view also, although there are many cases in which gastric mucosa appears in diverticula that do not seem to be inflamed. However, in every case in which the position of the aberrant tissue is stated, it is always at the apex, where the vitelline duct begins to atrophy and to constrict. Whatever causes this atrophy and constriction certainly would cause some irritation to the underlying endoderm. If such irritation actually were present in the embryo its influence could easily be outgrown.

Albrecht and Fischl look on this gastric mucosa as arising from misplaced fetal inclusions or rests. This view is similar to that offered in explanation of many foreign growths. In recent years Schaetz has been the chief proponent of this theory. Such a theory is difficult to prove or disprove. However, if the theory is true it seems strange that except in Meckel's diverticulum, where gastric mucosa has been reported many times, no cases (Taylor) have been reported in which congenital gastric mucosa has been found below the duodenum. Apparently other factors must be concerned.

Taylor in 1927 found some gastric mucosa in the ileum 10 inches (25.4 cm) from the ileocecal valve. He emphasized the fact that it was located on the mesenteric side, which fact he believed proves that it is not a part of Meckel's diverticulum. In view of its embryologic formation one would, of course, expect the remains of the vitelline duct to be found on the antimesenteric side, as is usually the case. However,

## COMMENT

While it has been known since 1861 that pancreatic tissue may occur in Meckel's diverticulum, the knowledge of the occurrence of gastric mucosa is of comparatively recent date (1904). That this gastric mucosa is active in producing a secretion similar to, if not identical with, the gastric juice of the stomach and containing both pepsin and hydrochloric acid has been shown several times in cases in which gastric mucosa has been seen at the umbilicus in polyps and fistulas (Telling, Stone, Taylor, Lexer, Hudson and von Rosthorn), and in a Meckel's diverticulum (Schaff). Such polyps and fistulas are, like Meckel's diverticulum, anomalies resulting from failure of the vitelline duct to undergo normal involution at about the 7 mm embryonic stage. It is therefore reasonable to assume that the gastric mucosa found in Meckel's diverticulum is also quite active in secreting pepsin and hydrochloric acid and that this secretion increases at mealtime, just as that in the stomach and umbilical fistulas is known to do. Such a secretion comes at a time when the small intestine and Meckel's diverticulum are relatively empty and the alkaline intestinal juice is not being formed. The acid gastric juice can accordingly act on the intestines undiluted, and it is not remarkable that ulcers are not uncommonly associated with this aberrant gastric mucosa. This is the explanation advanced by Lindau and Wulff for the formation of these ulcers.

Hudson and Koplik found that 67 per cent of their diverticula contained gastric mucosa. All their specimens were pathologic, and there can be little doubt but that the presence of much gastric mucosa is certain to be associated with some pathologic change. Their percentage, accordingly, must be higher than for the general incidence. Koch in 1912 found that six of fifty diverticula examined contained gastric mucosa, Schaetz in 1925 noted gastric mucosa in five of thirty specimens studied. In the nonpathologic specimens collected for this report there is gastric mucosa in but one of fourteen diverticula examined. The average of the last three series indicates an incidence of about 13 per cent.

Although the presence of pancreatic tissue in Meckel's diverticulum has been recognized for about seventy years, its occurrence is not very common. The only available statistics on the incidence of this aberrant tissue in this location are those of Schaetz, who found pancreatic tissue in three of thirty diverticula examined, and Koch who found it in two of fifty specimens. An average of these two series gives an incidence of 6.3 per cent, which seems too high in view of the relatively infrequent reference to such a condition in the literature.

The primitive digestive tube consists of an endodermal epithelial lining and a layer of mesoderm forming the splanchnopleure. Originally the cells of this endoderm are structurally identical throughout and from them are developed in the fetus the epithelial lining of all the parts of



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Von Rosthorn found tissue which to him resembled that of the parotid gland in a case of umbilical fistula. The occurrence of such tissue is difficult to explain, since the parotid gland is probably of ectodermal origin. It is possible that what he found was really pancreatic tissue.

As both islets and acini come from the same primordia, it is not surprising that several authors have specifically mentioned finding islets in the aberrant pancreas.

Case 11, that of the specimen with protrusions, while not without precedent in the literature, is unusual. Cullen collected reports of several cases of what he termed hernial protrusions. This term is particularly apt in view of the microscopic study of my case, in which the mucous membrane lacks a muscular coat and looks as if it might have pushed its way through this layer. Cahill described a diverticulum with three "tit-like projections on it." Kelynach found several specimens with "secondary lateral dilations" and some with "nipple-shaped projections." Doepfner published five illustrations of diverticula showing projections.

Practically every type of anomaly resulting from failure of all or part of the vitelline duct to become obliterated has been described. In some cases the distal part of the duct fails to atrophy, which results in an umbilical fistula or polyp. In rare cases the whole duct fails to retrogress, and a patent umbilical fistula results. Sometimes Meckel's diverticulum has a thin fibrous strand attached to its distal end where atrophy started but was incomplete. This fibrous strand may be free in the abdominal cavity, or attached at the umbilicus or attached to some abdominal organ.

Giant diverticula, while rare, are reported in the literature. Diverticula over 50 cm long have been described (McMurrich and Tisdall, Edmunds, Moll and Edwards), as well as one which filled almost half of the abdomen (Yates). McMurrich and Tisdall expressed the belief that certain of these large diverticula represent the remains of both the vitelline duct and the yolk sac. It is thought that the persistent stalk and sac are drawn into the abdomen by the intestines when they return from the celom of the umbilical cord. Christie and Doepfner reported terminally bifurcated diverticula.

In addition to the stomach and Meckel's diverticulum, other portions of the gastro-intestinal canal have been described as having at least in part a lining of gastric mucosa. Nicholson stated that cardiac epithelium is found in 75 per cent of persons in the esophagus at the level of the cricoid cartilage. This same investigator stated that in some cases inflammation in various parts of the intestinal tract causes a metaplasia of the epithelium resulting in the formation of gastric glands. In support of this theory he offered the evidence from seventeen cases in which a gallbladder removed for cholecystitis or cholelithiasis contained mucous

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Doepfner's figures give one diverticulum each in one hundred and two males and two hundred and fourteen females Hilgenreimer placed the figure at one in sixty-one females and thirty-nine males

As some of the foregoing data come from autopsy reports and since in general more males are brought to necropsy than females, this figure is perhaps a little too high However when the figures from the operating room are studied, where the numbers of patients of the two sexes are more nearly equal there remains little doubt that Meckel's diverticulum occurs more often in males than in females This disproportion in sex distribution of gastric mucosa in cases of Meckel's diverticulum accords roughly with that for gastric and intestinal ulcers

The only instance in the series reported here in which the position of the diverticulum was determined was one in which it was situated 100 cm above the ileocecal valve This is the upper limit as given by most authors Foerster gave the upper limit as 4 feet (121.9 cm) above

TABLE 6—*Distribution of Meckel's Diverticulum as to Sex*

Author	Male	Female
Schaetz	9	8
Kettler	91	18
Mitchell	33	4
Christie	50	13
Hudson and Koplik	30	15
Wellington	201	64
Kelynach	11	7
Sandlos	3	9
Total	432	138
Proportion	31	1

the cecum Fitz placed the position at 12 inches (30.5 cm) above the valve in the new-born and 3 feet (91.4 cm) in the adult In Kelynach's eighteen cases the upper limit was 50½ inches (128.8 cm) the lower limit, 15 inches (38.1 cm), and the average 34½ inches (87.6 cm) which is approximately the figure that is usually given for its position, namely, 3 feet In Hudson and Koplik's series of thirty-two cases the diverticula ranged from 8 to 40 inches (20.8 to 101.6 cm) above the ileocecal valve Christie in a series of sixty-three cases, found the upper limit to be 90 cm above the cecum, the lower limit, 15 cm, and the average, 50.6 cm

The question arises as to how these heterotopic growths in the remnants of the vitelline duct are to be explained Since gastric mucosa was first found in the umbilicus the earlier attempts at explanation were concerned with aberrant tissue in this location

Tillmanns in 1882 first found gastric mucosa at the umbilicus He looked on this mucosa as the remains of a gastric diverticulum which projected through the umbilicus and the connection of which with the

# THE INJECTION OF EOSIN INTO THE KNEE JOINT

## ITS VALUE IN ARTHROSCOPY

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I have previously indicated<sup>1</sup> that eosin tends to stain eroded areas in cartilage selectively, that is, the lesion in the cartilage is stained, but the surrounding normal cartilage is not. I know that this is true of such lesions in tissue examined soon after death. In experimental arthritic lesions produced in the knee joints of rabbits<sup>2</sup> by traumatization of the cartilage of the knee joint with a large bore needle, no selective staining was observed with eosin or with any other dye used. The intensity of staining varies with the concentration of the dye, and the critical concentration at which the synovial membrane stains and the cartilage does not was observed to be a 0.05 per cent aqueous solution of eosin. Since I knew of no other dye with apparent selectivity, I have used only eosin for clinical work.

The pharmacologic behavior of eosin may account for its action on intra-articular injection. It is an acid dye which shows no selective affinity for any particular tissue group by any method of administration, least of all for fat or nerve tissue. Yet a greater receptivity for the dye by damaged or dead tissue cells had been noted, and this was stressed by Rost<sup>3</sup>. Folkmar<sup>4</sup> made this interesting statement: "Just why a living cell is stained by a neutral or basic dye, while a dead cell is stained by an acid dye, is still problematic."

This must be, then, the pharmacologic peculiarity of eosin which makes it selective for diseased areas in cartilage. Yet since eosin is a dye without specific affinity, it may occasionally stain normal cartilage, and in fact it does. But it is observed that the depth of staining of diseased parts is greater than that of any normal part.

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3 Rost, E. Wirkungen des Eosins auf Tiere. II. Pharmakologische Untersuchung des Eosins, mit Berücksichtigung der Wirkungen des Fluoreszeins und Erythrosins, *Arch. d. Ges. dtsch. Arb.* **40** 171, 1912.

4 Folkmar, E. A. Selective Action of Dyes Used in Medicine. A Historical Review, *J. Radiol.* **6** 213, 1925.

McMurrich and Tisdall described several cases which suggest that it can arise from the mesenteric border. They mentioned the case of Robertson which has not yet been reported, in which the diverticulum arose from the ileum on its mesenteric side 20 cm from the ileocecal valve. Edmunds reported a case in which the diverticulum ran 40 cm through the mesentery. In an 18 year old girl, Reed found a diverticulum which arose from the mesenteric border of the intestine. Abt and Strauss found a diverticulum which was located between the layers of the mesentery and which arose from the mesenteric border. Accordingly, it appears probable that Meckel's diverticulum can and sometimes does arise from the mesenteric side of the intestine and that the case of Taylor represents the remains of a very small Meckel's diverticulum. Except for this case and the cases of Nicholson, which he believed to be due to inflammation, no cases of gastric mucosa occurring in the small intestines proper could be found.

The stomach, esophagus and whatever remains of the vitelline duct grow relatively slowly as compared with the intestines, which, during the stage when the gastric glands are being differentiated from the primitive endoderm (middle of the second month), are growing so rapidly that they are forced to occupy the celom of the umbilical cord. It seems particularly significant that gastric mucosa has been reported in each of these slow-growing regions of the digestive tract but not in the faster-growing ileum and jejunum. This theory was originally proposed by Stone in 1923, with a statement that the rapid growth of the intestines inhibited the "high degree of differentiation found in gastric mucosa."

Briefly, there are two chief theories in explanation of the occurrence of gastric mucosa in the remains of the vitelline duct.

1 The gastric mucosa represents dislocated fragments of tissue engrafted in the vitelline duct.

2 The simpler and more obvious explanation is that the primitive endoderm, which possesses the pluripotentiality of developing into any one of the several types of epithelium or glands of the digestive tract, is stimulated locally in some undetermined manner to develop into a tissue anomalous for a particular region. Such stimulation has been thought to be irritation, inflammation, lack of bile and relatively retarded growth at certain levels. It appears probable that any or all of these factors may be operative in variable degree.

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on the under-surface of the patella seen through the arthroscope, stained a greenish color, bordered by a ring of red-pink. No note was made regarding the staining of cartilage elsewhere. In a man, aged 27, in whom this disease was localized solely in the synovia, the normal cartilage did not stain, this was also noted in the opened joint. Uniform light staining of the synovia and of the cartilage occurred in a woman, aged 37, in whom synovectomy of the knee had been done more than a year before. A woman, aged 58, in whom arthroscopy alone revealed a villous synovitis and some opacity and fuzziness of the internal femoral condyle showed no staining of the cartilage of the femoral condyles. There was a similar experience in the case of a woman, aged 31, with chronic villous synovitis. The under-surface of the patella did stain a little in streaks. When synovectomy was done on this joint a week later, no dye was seen in the joint. No erosions of the cartilage were seen, and the cartilage in general was a bit more yellowish and fuzzier than is normal.

In the one tuberculous knee, into which the dye was injected preceding fusion of the knee, there was noted a uniform, light pink staining of the synovia, especially of the quadriceps pouch. Several erosions of the femoral condyles had picked up the dye, but several others, which were even larger, had failed to do so. The reason for this was that they were covered by an adherent and inflamed synovia which did not allow contact with the dye. The normal cartilage over the midpart of the femoral condyles did not stain but showed a mild pink.

In none of these cases was an attempt made to determine the  $p_H$  of the joint before and after injection or the  $p_H$  of the eosin injected. I conferred with Dr. Aaron Bodansky, chemist of the Hospital for Joint Diseases on this particular point. It is not possible to use the indicator method in determining the  $p_H$  of the eosinized fluid, and special apparatus is necessary. It is a point worth investigating. Eosin is an acid dye. Any selectivity it may possess should be due to a basic reaction of eroded areas in cartilage.

The reaction of the synovial fluid varies in health and disease. An interesting study by Borghi<sup>5</sup> is pertinent. Using the method of Rous,<sup>6</sup> who had found that certain indicators injected intravitaly appeared in the joint fluid, Borghi injected phenol red intravitaly in an effort to study the actual reaction of the intra-articular tissues under various conditions, especially the reaction of joint cartilage. Thus, he noted that heat applied to a joint produced alkaline changes, cold applications gave a light and inconstant acidity. Long duration of

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# THERMAL CHANGES IN LOCAL ASPHYXIA AND REACTIVE HYPEREMIA

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It has been known for a little more than fifty years that after local asphyxia there occurs a local vasodilatation, which is nearly a maximal response of the vessels involved provided that the asphyxia has been of sufficiently long duration. The immediate cause of this vasodilatation is unknown. This phenomenon is of frequent occurrence and is of great value to the tissues from a protective standpoint, since it is obvious that in terrestrial life the standing, sitting or lying posture must lead to anemia of the weight-bearing tissues and therefore to a reactive vascular dilatation whenever the static force has been of appreciable duration, perhaps longer than one second<sup>1</sup>. It is obvious that a local anemia is accompanied by increased loss of heat provided that the surrounding climate is cooler than the temperature of the anemic part. This paper is concerned with a quantitative study of the thermal effects in local asphyxia and recovery.

## REVIEW OF THE LITERATURE

The term reactive hyperemia was first used by Bier<sup>2</sup> to describe the intense hyperemia of the skin following vascular stasis in the extremity. The most fruitful studies of the problem have been made by the use of various mechanical devices to constrict the blood vessels and observation of (1) the bright arterial flush in the skin, (2) changes in the volume of the tissues, (3) the rate of inflow of blood following release and (4) changes of systemic blood pressure.

Although it may have been previously observed by physiologists, the first clear description of the phenomenon was made by Cohnheim,<sup>3</sup> who

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1 Goldblatt, H. *Heart* **12** 281, 1925

2 Bier, A. *Virchows Arch f path Anat* **147** 256, 1897

3 Cohnheim, J. *Untersuchungen über die embolische Prozesse*, Berlin, A. Hirschwald, 1872

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strenuous exercise and somewhat greater than the vasodilatation following exposure to heat. Thus occlusion for ten minutes was followed by greater and more prolonged hyperemia than soaking in water at 44 C for thirty minutes. Studies of the volume of the limbs suggested that hyperemia occurred in all the tissues. Study of the rate of inflow of blood showed that dilatation occurred during the obstructive phase. These workers also presented strong evidence that the arterioles and capillaries are the chief vessels responsible for the hyperemia. After the removal of a tourniquet the cutaneous hyperemia did not extend as much as 1 mm beyond the asphyxiated areas. Lewis considered the nature of the vasodilating agent and stated that the effect is probably due to the formation of slowly diffusible metabolites in the extravascular spaces. Bier<sup>13</sup> also concluded that the larger vessels are not involved in the hyperemia. Goldblatt<sup>1</sup> showed that skinning the leg did not abolish this increase of volume of the limb following the release of circulatory arrest.

Krogh<sup>14</sup> presented evidence that lack of oxygen is not the primary factor necessary for the development of the vasodilating substance. He noted by direct observation of the capillaries that completely anemic areas responded to asphyxia by dilatation.

No data are supplied in the present paper concerning the nature of the vasodilating substance. The older work on this subject was reviewed by Fleisch,<sup>15</sup> who stated that an increased acidity is responsible for the increased flow of blood but that doubtless this is not the immediate mechanism responsible for dilating the vessels. The problem is a thorny one. Since normal blood readily acquires vasodilator properties, as was shown by the work of Phemister and Handy,<sup>16</sup> great care is necessary in interpreting data acquired by perfusion methods about such a delicate reaction as reactive hyperemia.

Thermal changes in an extremity in which circulation was arrested were studied by Bazett and McGlone,<sup>17</sup> using the thermocouple method. These workers showed that during stasis there is a definite but very gradual cooling of the tissues, and on release the previous temperature is regained and a still higher level is attained as the result of reactive

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13 Bier, A. *Zentralbl f Chir* **51** 2, 1924

14 Krogh, A. *The Anatomy and Physiology of Capillaries*, New Haven, Conn., Yale University Press, 1922

15 Fleisch, A. *Ztschr f allg Physiol* **19** 269, 1921

16 Phemister, D B, and Handy, J. *J Physiol* **64** 155, 1927

17 Bazett, H C, and McGlone, B. *Studies in Sensation. Chemical Factor in Stimulation of End-Organ Giving Temperature Sensations*, *Arch Neurol & Psychiat* **28** 71 (July) 1932

Rost and others have adequately demonstrated the absence of toxic effects following the administration of eosin by various routes, and this observation is not denied by my experience with the dye

I injected from 10 to 20 cc of a 0.05 per cent aqueous solution of eosin into eleven joints in seven of which the injection was made subsequent to arthroscopy. In a twelfth case a 0.5 per cent aqueous solution of eosin was accidentally injected into the knee joint, and intense diffuse staining of both synovia and cartilage, both of which were normal, was observed through the arthroscope. Visualization of this joint after staining with so strong a solution was poorer than visualization with the unaided eye. Yet no irritation of the joint was noted.

The solution was sterilized before injection, injected in proper amount and immediately reaspirated or flushed out with physiologic solution of sodium chloride or Ringer's solution. Staining was always immediate and superficial. The dye caused no irritation whatsoever to the joint and was rapidly absorbed, so that in the two cases in which arthrotomy was done no trace of the dye nor any irritation from it was seen a week later.

It is not necessary to inject eosin into a joint for clear vision at arthroscopy. Yet the dye does make the synovia stand out more clearly, and other structures are better seen. The joint space is stained a fluorescent green, into which a few fine bluish-green synovial villi may be seen floating. The synovia usually stains a light pink, and the villi are clearly outlined against the unusual background of the fluorescent joint space.

It has been my problem to decide definitely whether this dye stains eroded areas in cartilage selectively.

In three cases in which operation was done for the removal of a torn meniscus, the following findings were observed:

In one case it was seen through the arthroscope that the relatively normal femoral cartilage did not stain, although it did have a pinkish tinge. An erosion on the under-surface of the patella was stained deeply. The internal meniscus stained a fluorescent green. At arthrotomy, a week later, no dye was seen in the joint and the surgeon did not examine the under-surface of the patella. In another case, the synovia and the normal cartilage within the joint were stained uniformly. The most interesting case in this group was that of a man of 22 with a tear of the posterior part of the internal meniscus and an erosion of the internal femoral condyle. This eroded area was stained a delicate pink, which clearly delineated it. The joint, which was opened immediately after arthroscopy, showed that this eroded area had stained fairly well but that certain areas in the normal cartilage had stained too. In a youth, aged 17, with osteochondritis dissecans of the external femoral condyle, the normal cartilage had not stained, and the area of dissected cartilage had stained a light pink.

The following findings were noted in six cases of chronic villous synovitis in which the joint cartilage showed little or no change:

In a woman, aged 22, in whom the dye was injected into the joint just before arthrotomy and allowed to remain in the joint for five to ten minutes, there was uniform staining of both cartilage and synovia. In a youth, aged 18, an erosion

## RESULTS

EXPERIMENT 1—*Thermal changes in complete asphyxia of limb resulting from mechanical constriction*

An inflatable cuff of the Riva-Rocci type was placed around the mid thigh of a man, and thermocouple loops were placed on the skin over each ankle and knee and above the constrictor. After a preliminary determination of the temperature the cuff was inflated to a pressure equivalent to 50 mm of mercury above the systolic blood pressure and maintained for twenty-five minutes. The results in this case, typical of those obtained in twelve determinations in four subjects, are shown in chart 1. In the constricted leg there was a greater fall in temperature of the knee than in that of the ankle, a slow but steady rise of the temperature occurred in the control leg and above the tourniquet in the experimental limb. At

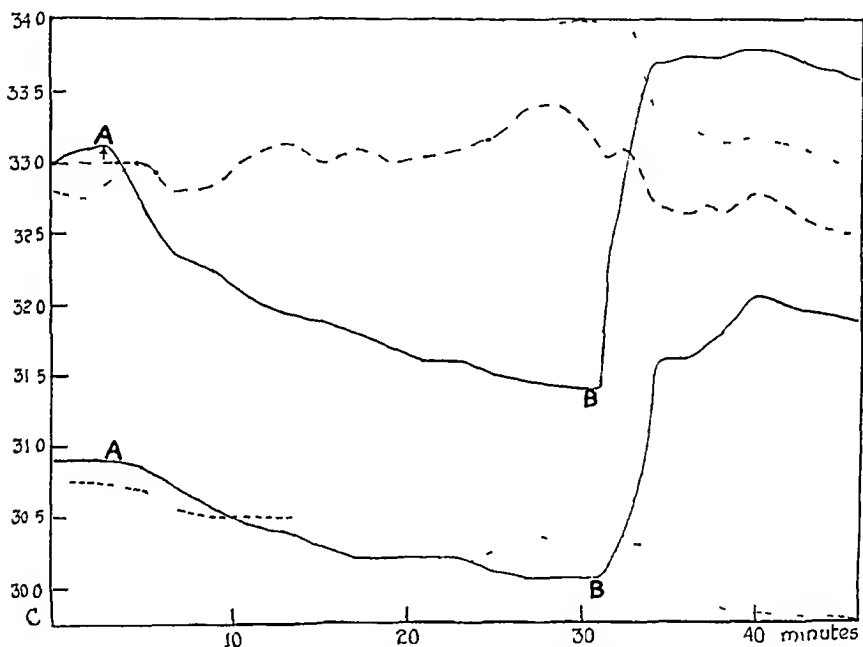


Chart 1 (subject B H B) —A tourniquet was applied for twenty-five minutes on the left mid thigh with thermocouples on the skin over the ankle and knee of each leg and above the constrictor on the left leg. The graph shows the lowering of the temperature in the obstructed area with hyperthermia following release. A rise of the temperature in the control areas during the period of obstruction followed by a decrease on the removal of the tourniquet is also shown. The solid lines indicate the changes in temperature at the left medial condyle (upper line) and at the left internal malleolus (lower line). The broken lines indicate the changes in temperature at the right medial condyle (upper line) and at the right internal malleolus (lower line). The broken line with dots indicates the change of temperature on the left thigh above the tourniquet. A and B indicate the time of application and of removal of the tourniquet.

the time of release, there occurred a large increase in temperature above the initial readings in the constricted leg and a sharp fall in the temperature of the control areas.

immobilization produced acid changes, whereas the labor of passive mobilization or of primary motion gave alkaline changes. The changes of disease seldom lower the  $p_H$  of the joint fluid lower than 7, according to Seeliger.<sup>7</sup> The protective effect of the oily synovial fluid may retard the staining of the cartilage.

These fundamental theoretical points must be appreciated and completely elucidated before the effects of staining of the joint cartilage by dyes can be fully understood. The paths of absorption of materials injected into joints, especially the knee joint, have been fairly well worked out.

From a practical standpoint, it can be stated, even from this small series of cases, that eosin can cause diffuse staining of normal cartilage and synovia, that, while erosions of various etiology on cartilage will stain selectively with eosin, normal cartilage in the presence of these erosions will also stain, usually in spots. The visualization of an eroded area is made clearer by the use of the dye. Lightly altered cartilage without erosion usually does not stain. Greatly degenerated cartilage stains diffusely.

Since the dye is nonirritating and since it clarifies vision, I see no reason why it should not be used in properly selected cases as an adjunct to arthroscopy.

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<sup>7</sup> Seeliger. Ein Beitrag zur pathologischen Physiologie der Gelenke unter Berücksichtigung der Gelenkmausbildung, *Arch f klin Chir* **142** 606, 1926.

other in a lowered position for five minutes. The cuff was inflated, and the legs were subsequently maintained in a horizontal position. In each instance, as shown in chart 4, there was a greater rise in temperature following release in the leg which had been elevated, and which was pale and relatively anemic, than in the congested leg.

EXPERIMENT 2—*Thermal changes in the partially asphyxiated limb*

In the tests on human subjects a Riva-Rocci cuff on the thigh was distended to diastolic pressure and allowed to remain in place for thirty minutes. To obtain an estimate of the amount of blood leaving the leg, 6 mg. of phenolsulfonphthalein (phenol red) was injected into a dorsal vein in the foot immediately after distention of the cuff. The subject voided urine just before the removal of the tourniquet, and the amount of excreted dye was compared with a similar volume of phenolsulfonphthalein excreted under identical conditions without vascular con-

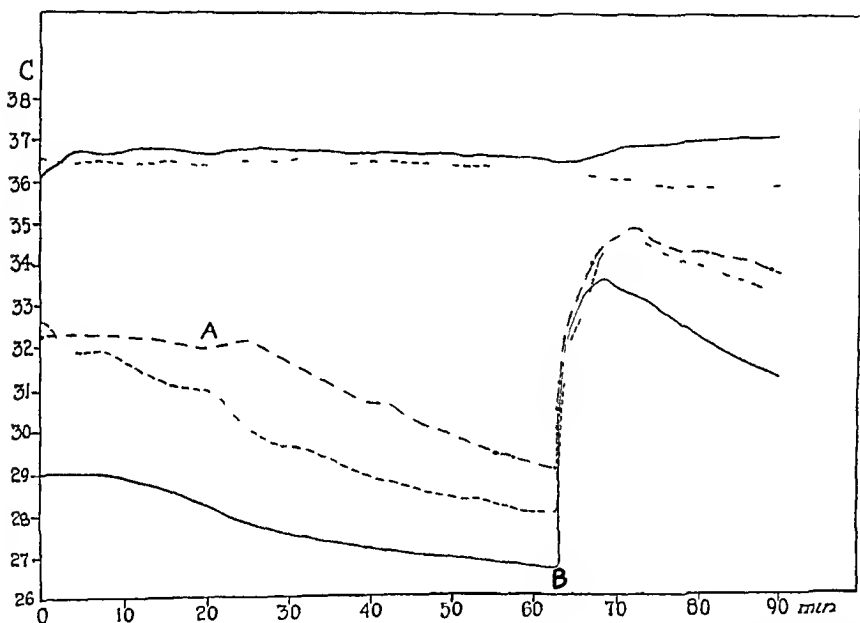


Chart 3 (rabbit 70) —A tourniquet was applied to the right thigh with thermocouples in the marrow of the tibia and the metatarsal bones and in the subcutaneous tissue in the lower part of each leg. The fall in temperature in the control areas and the hyperthermia in the experimental leg on the removal of the obstruction are demonstrated. The solid lines indicate the changes in temperature in the marrow of the right femur above the tourniquet (upper line) and in the marrow of the right metatarsal bones (lower line). The broken lines indicate the changes in temperature in the marrow of the left femur (upper line) and in the marrow of the right tibia (lower line). The broken line with dots indicates the change of temperature in the subcutaneous tissue of the lower part of the right leg. A and B indicate the time of application and of removal of the tourniquet.

striction. It was found that amounts varying from a trace to 18 per cent of the amount excreted in the control experiment were excreted, showing that the amount of fluid leaving the partially constricted leg is small. As is shown in chart 5, the temperature fell slightly in the congested leg and continued to fall after the removal

observed flushing after the removal of a ligature applied to the tongue of a frog Roy and Brown<sup>4</sup> in experiments on the web of the frog's foot observed that there was dilatation of arterioles and capillaries following anemia, that the effect was more marked when the anemia had been of longer duration and that it occurred when the sciatic nerve had been cut That the hyperemia is of greater magnitude and of longer duration the longer the period of circulatory arrest, within an upper limit, was first observed by Lister<sup>5</sup> and has since been proved by others<sup>6</sup> Bayliss<sup>7</sup> and others<sup>8</sup> showed that equal periods of occlusion are followed by approximately equal degrees of hyperemia

Bier<sup>2</sup> showed that reactive hyperemia is a local effect on the tissue occurring independently of the content of blood in the extremity and of the nervous system in man and in the pig This worker amputated the leg of a pig, except for the femoral vein, and connected the cut ends of the femoral artery with a glass cannula Obstruction of the flow of blood through the cannula for five minutes was followed by a strong hyperemic flush in the skin This observation was confirmed by Goldblatt<sup>1</sup> In the pig Bier excised the dorsolumbar portion of the spinal cord, sectioned both sympathetic chains and then clamped the aorta for five minutes, a strong hyperemia occurred on reestablishment of the circulation Lewis and Grant<sup>9</sup> showed in man that reactive hyperemia occurred in skin wherein the nerves had degenerated, and this has been confirmed<sup>1</sup> for the dog

Bayliss<sup>10</sup> found that arterial obstruction in the denervated limb caused a decrease in the volume of the limb and that removal of the obstruction was followed by an increase in the volume of the limb and a fall of general blood pressure Von Anrep<sup>11</sup> confirmed this observation and showed that if the main artery and vein of the limb were clamped the leg did not decrease in volume but that following release swelling of the limb occurred

Ingenious experiments devised by Lewis and Grant<sup>12</sup> showed that reactive hyperemia is due to a great dilatation of the involved blood vessels and that it is only slightly less than the changes occurring in

4 Roy, C S., and Brown, G J *Physiol* 2 323, 1879

5 Lister, I *Brit M J* 1 923, 1879

6 (a) Tomita C *Arch f d ges Physiol* 116 299, 1907 (b) Lewis T, and Grant, R *Heart* 12 73 1925 (c) Goldblatt<sup>1</sup> (d) Bier<sup>2</sup>

7 Bayliss, W M *J Physiol* 28 220, 1902

8 (a) Tomita<sup>6a</sup> Lewis and Grant<sup>6b</sup> Goldblatt<sup>1</sup>

9 Lewis T and Grant R T *Heart* 12 209, 1924

10 Bayliss W M *J Physiol* 26 29, 1901, footnote 7

11 von Anrep, G *J Physiol* 45 318 1912

12 Lewis and Grant (footnotes<sup>6b</sup> and<sup>9</sup>)



of the constriction, and this was not accompanied by hyperthermia, indicating that a much smaller hyperemia occurred than in the completely obstructed leg

EXPERIMENT 3—*Thermal effects of the injection of large doses of epinephrine into the main artery of a limb of the dog*

In order to determine whether the musculature of the blood vessels is paralyzed or not, this experiment was devised and carried out on dogs. Thermocouples were inserted in the muscles of each leg and over the sternum, and with the area under procaine hydrochloride anesthesia the femoral artery was exposed in each groin. A rubber tube constrictor was applied as high in the thigh as possible for twenty minutes and then removed, and 0.5 cc of a solution of epinephrine hydrochloride (1:1,000) was injected into the femoral artery as quickly as possible. As may be seen in chart 6, which shows results typical of those obtained in the

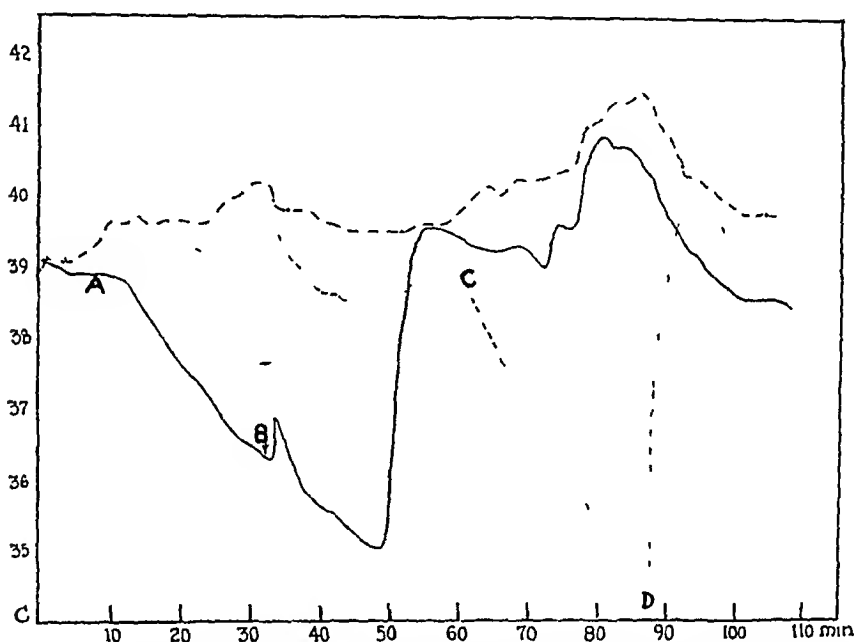


Chart 6 (dog 132)—Mechanical constriction of the left thigh for twenty-two minutes was followed by the injection of 0.5 cc of Ringer's solution into the right femoral artery. The broken line with dots indicates the changes of temperature in the chest wall. The broken line indicates the changes of temperature in the right leg, and the solid line indicates the changes in temperature in the left leg. At A the tourniquet was applied to the left thigh, at B the tourniquet was removed, and epinephrine hydrochloride was immediately injected into the femoral artery, at C the tourniquet was applied to the right thigh, and at D it was removed, and Ringer's solution was immediately injected into the femoral artery.

four experiments made, during the period of mechanical constriction the typical fall of temperature occurred. During the period of injection of epinephrine a slight rise occurred, obviously due to warm blood entering the leg, but this was quickly followed by a further lowering of the temperature at the same rate as with mechanical constriction for eighteen minutes, when a temperature above the initial readings occurred. In order to evaluate the effect of mechanical inter-

hyperemia The published data of these workers have been few and do not include a complete thermal record during and after vascular occlusion Hintze<sup>18</sup> studied thermal effects following the application of a tourniquet by means of a mercury thermometer held in the fingers and concluded that the elevation of the temperature amounted to about 0.5 C (0.9 F) above the initial reading and that it persisted for approximately two hours This worker, as well as many others showed that cooling of the tissues is not the causative agent of the dilatation

#### METHODS

Most of the observations were made on man, although the dog and the rabbit were also used Unless it is stated that anesthesia was used, the subjects were not anesthetized All determinations of heat were made with a thermo-electric couple, the component elements of which were copper and constantan The reference junction was kept in a Sheard constant temperature bath<sup>19</sup> The variable junctions were of three types All observations on the skin were obtained with loops of no. 30 gage copper and constantan wire kept in place on the surface of the skin by a rectangular piece of surgical adhesive tape about 2 by 0.5 cm The temperature of the muscles was obtained by soldering 44 gage insulated copper and constantan wires into a 26 gage steel hypodermic needle To obtain the temperature of the bone marrow couples were constructed of 34 gage insulated wires, twisted for about 2 cm and soldered at the end, which were inserted into the marrow cavity after puncture of the superficial tissue and the bone with a large (18 gage) hypodermic needle These punctures were made in the rabbit during brief ether anesthesia A definite lack of resistance was noted when the needle entered the marrow cavity, and blood appeared in the lumen, the couples then entered the marrow cavity to any desired depth, the needle was removed over the wires and the puncture wound was sealed with collodion The galvanometer<sup>20</sup> was of the D'Arsonval type, with a sensitivity of 0.004 micro-amperes per millimeter at a distance of 1 meter, a period of four and four-tenths seconds, a damping resistance of 280 ohms and a coil resistance of 41 ohms The thermocouple circuit,<sup>21</sup> including the galvanometer and switches, was composed entirely of copper except for the relatively short section of constantan between the reference and the observation junction A resistance of 350 ohms in addition to thermocouples, switches, etc., was inserted in the circuit This gave a deflection of 1.9 cm per degree centigrade at a distance of 1 meter, and the limit of accuracy of the instrument was 0.05 C (0.09 F) The ensemble was repeatedly calibrated against a mercury thermometer, water of known temperature being used in a Dewar flask

All the experiments were conducted in a quiet, warm (21 to 26 C) room Psychrometric determinations of temperature and relative humidity were made The experimental animals were placed on a table for a preliminary resting period of from ten to ninety minutes preceding all experiments, and throughout the period the table was insulated with blankets to minimize artificial loss of heat

18 Hintze, A. *Deutsche Ztschr f Chir* 234 172, 1931

19 Sheard, C. *Am J Chn Path* 1 209, 1931

20 Leeds and Northrop, type R, 2,500 C

21 Dr Paul C Foster, of Tulane University aided in the design and construction of the circuit

blood came from the wound. The vessels became occluded with blood clots, so that after the constricting effects of the epinephrine had worn off there was no bleeding. At the end of this two hour period the normal leg was amputated at the same site without hemostasis and without injection of epinephrine, the dog died in sixteen minutes of anemia, having lost 293 cc of blood. This evidence is rendered as proof that injection into the femoral artery of relatively large amounts of epinephrine causes complete vasoconstriction and renders the tissue supplied by the artery essentially bloodless.

EXPERIMENT 4—*Thermal effects of injection of large doses of epinephrine into the main artery of a limb in man*

In three men a relatively large dose (0.5 to 0.75 cc) of epinephrine hydrochloride (1:1,000) was injected into the femoral artery just below the inguinal

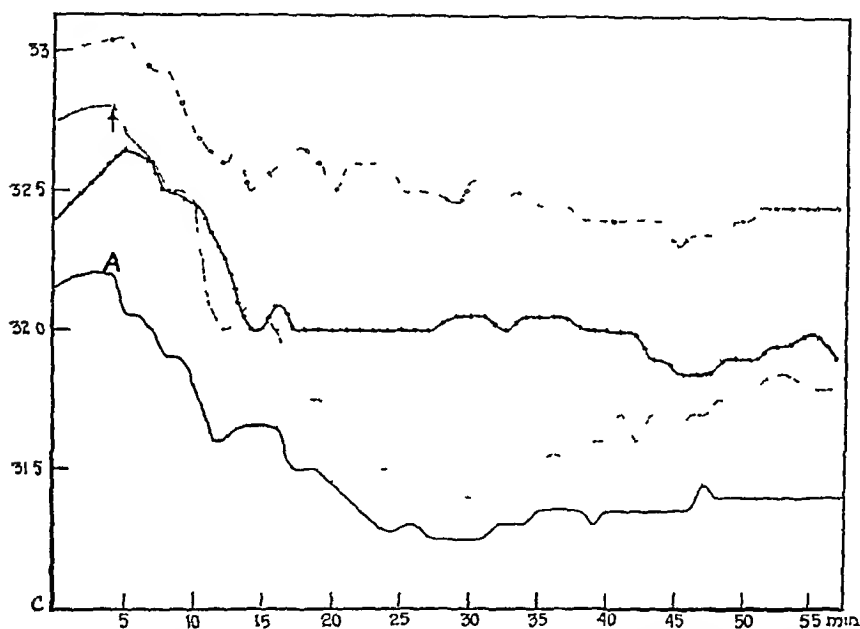


Chart 8 (subject M O) —Cutaneous temperature readings over both ankles and knees after the injection of epinephrine hydrochloride solution into the right femoral artery. Reading from the top down the lines indicate the changes in temperature in the left medial condyle, the left internal malleolus, the right medial condyle and the right internal malleolus. At A, 0.75 cc of epinephrine hydrochloride (1:1,000) was injected into the right femoral artery.

ligament. In subject M O (chart 8) there was a rise in the systemic blood pressure of 68 mm of mercury in four minutes, accompanied by tachycardia and slight dyspnea. The experimental leg became cadaveric in its waxy-white appearance, and there was complete obliteration of the pulses in the dorsalis pedis and posterior tibial arteries. There were few unpleasant sensations in the anemic leg, and cooling occurred. The recovery began in about twenty-five minutes after the injection; there developed in the skin a circumferential band of hyperemic flush about 15 cm in length which appeared first in the mid thigh and progressed in a bandlike fashion to the foot. As the hyperemic band progressed centrifugally,

Essentially similar results were obtained in six dogs and four rabbits. In these animals an area in the lateral aspect of the upper part of the thigh was infiltrated with procaine hydrochloride, and the anesthetized area was transfixed with a steel pin to hold in position a thin rubber tourniquet used to obtain stasis. Greater thermal changes, both of cooling and of heating, were obtained in these animals than in man, presumably owing to the lesser thermal capacity of the limb. In chart 2 a typical result is shown in a rabbit in which a thermocouple was placed in the marrow cavity of each tibia and in the muscles of the lower hindleg and each foreleg. It will be seen that the increase of heat following circulatory release is much greater in the bone marrow than in the adjacent muscles, and in all experiments the bone marrow was found to heat more than the muscle, the subcutaneous tissue or the skin.

In chart 3 thermal changes are shown in the obstructed leg of a rabbit in which thermocouples were inserted into the marrow cavity of the metatarsal bones, the

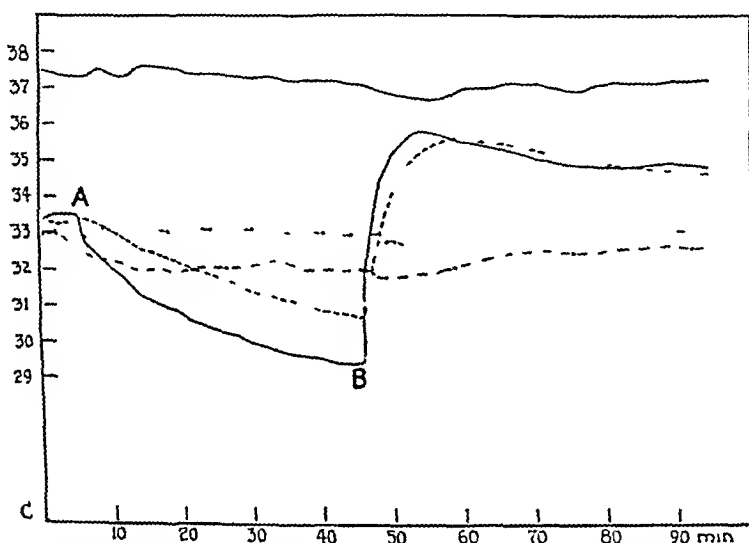


Chart 2 (rabbit 50)—A tourniquet was applied on the left thigh for forty minutes with thermocouples in the muscles and marrow of the lower part of the leg on both sides. The loss of heat during the period of obstruction followed by hyperthermia on release is shown. There was a slight drop in temperature of the control areas on release of the constriction. The solid lines indicate the changes in temperature in the right foreleg intramuscularly (upper line) and in the marrow of the left leg (lower line). The broken line indicates the changes in temperature in the muscle of the left leg. The broken dotted lines indicate the changes of temperature in the muscle of the right leg (upper line) and in the marrow of the right leg (lower line). A and B indicate the time of application and of removal of the tourniquet.

tibia and the femur. It will be observed that there was no fall of temperature of the cavity of the femur, and a roentgenogram showed that the couple had been inserted above the constrictor. The extent of the thermal changes brought about by stasis and release may be seen.

A series of six experiments were done on human beings. Before the constricting cuff was applied to the thigh one leg was maintained in an elevated and the

## COMMENT

It is obvious that circulatory changes can be profitably studied in the limb from a thermal standpoint provided a lower temperature exists in the laboratory than in the area studied. When the extremity the circulation of which was obstructed was kept at body temperature, there was no loss of heat. Since a very small amount of heat is produced in a quiet extremity, an increase of heat must mean an increased flow of blood from the interior of the body, and a rise of temperature in the quiet extremity therefore indicates an increased flow of blood. Cooling need not mean a decreased flow of blood, but it must be interpreted in the light of the following factors: (1) the thermal capacity of the tissue, which is related to the bulk of the limb and to the insulating capacity of the covering, especially subcutaneous fat, skin and hair (thus a small limb with thin insulation lost heat more rapidly than a limb in which the insulation was greater), (2) the temperature and moisture of the surrounding air, and (3) local sweating. Of these adventitious factors, the first two are eliminated by study of the corresponding normal extremity. Local sweating is the most difficult interfering factor to control and was of importance in some of the experiments with human beings, since several times before removal of the constricting cuff sweating was observed in the control extremities while the obstructed limb remained dry. In considering, then, the limitations of the method, especially with regard to sweating, which applied chiefly to man, it was found that the thermal events incident to circulatory release coincided with flush, limb volume and inflow methods previously used, provided the studies were made under controlled climatic conditions and with adequate control observations of the corresponding normal extremity.

The thermal data show that all the tissues in the extremity participate in the cooling during a period of mechanical obstruction and in the hyperthermia following release. It seems proved that hyperemia occurs in bone marrow and in muscle as well as in the skin, it may be seen from charts 2 and 3 that there was no lag in the increase of heat in the deep tissues, such as would be anticipated were the hyperemia confined to the skin, with conduction of heat producing elevation of the temperature of the deeper structures.

It was found that greater increments of heat occurred in the deeper tissues, especially in the bone marrow, than in the skin. This is at least partially accounted for by increased insulation of the deeper tissues, with less chance for loss of heat than in the skin.

The recovery from mechanical obstruction of circulation in the limb was in each case followed by hyperthermia when the duration of the arrest had been longer than fifteen minutes. In sharp contrast, in

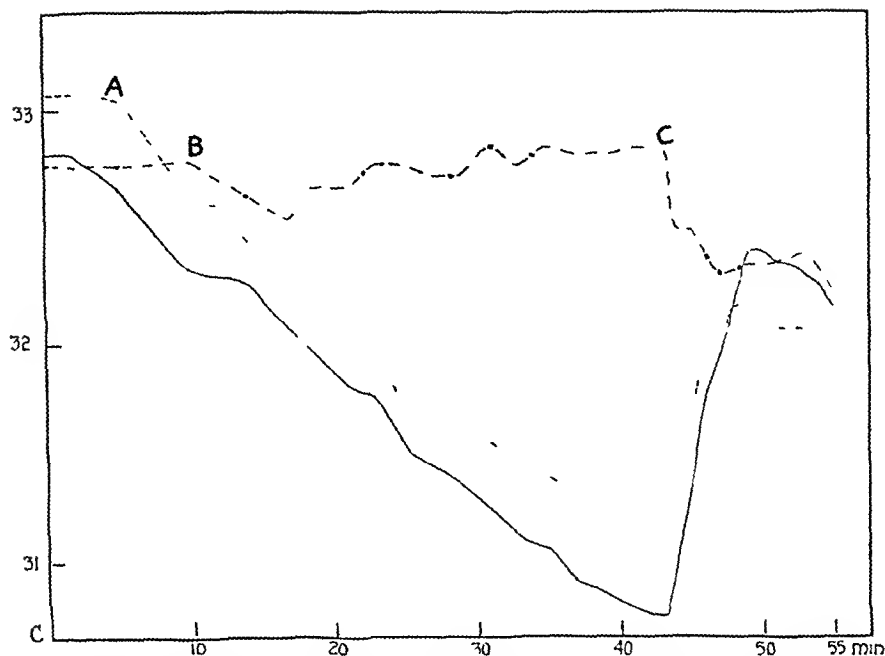


Chart 4 (subject M O) —Tourniquets were applied to both legs after the left leg had been elevated and the right leg lowered for five minutes. A greater degree of hyperthermia developed in the left leg than in the right. A fall of temperature of 0.5 C occurred in the skin of the upper part of the right arm after the release of the circulation. The broken line with dots indicates the changes in temperature in the right arm. The broken line indicates the changes of temperature of the right foot, and the solid line indicates those in the left foot. A indicates the time at which the left foot was elevated and the left foot was lowered. B indicates the time of application of the tourniquet and of returning both legs to the horizontal position, and C indicates the time of removal of the tourniquets.

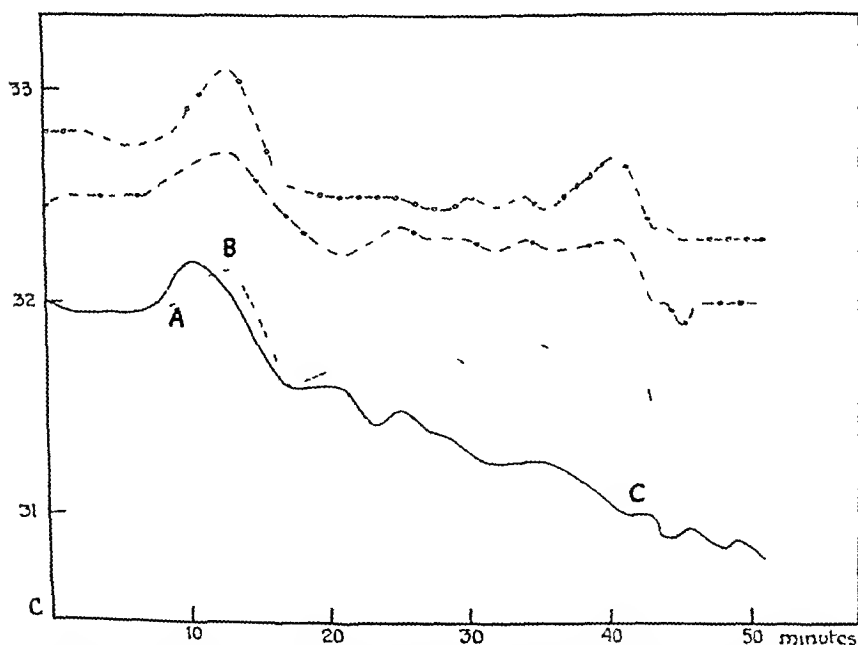


Chart 5 (subject C H) —Application of mechanical stasis at diastolic pressure (70 mm of mercury) on the left leg for thirty-one minutes was not followed by hyperthermia in the leg. The broken lines with dots indicate the changes in temperature in the left knee (upper line) and in the right knee (lower line). The broken line indicates the changes in temperature in the right foot, and the solid line indicates those in the left foot. At A the tourniquet was applied to the right thigh, at B phenolsulphonphthalein was injected into the right leg, and at C the patient voided urine, and the tourniquet was removed.

agrees with much previous work<sup>23</sup> which has indicated continued spasm of local blood vessels

The fall of temperature in the control areas when a mechanical tourniquet was removed from another limb has not been previously observed. This decrement, amounting to from 0.3 to 3 C (0.5 to 5.4 F), always occurred. It is undoubtedly related to the fall in systemic blood pressure and perhaps indicates vasoconstriction. It is not entirely due to the passage of blood through a cool limb. In a series of five experiments on man, mechanical arrest of circulation was produced in both legs with an inflated cuff while thermal changes in the arm were measured. At the time of arrest of circulation the obstructed limbs were covered with blankets and heated with electric lights, so that a great increase in local heat occurred (to 40 C [72 F]). When the tourniquets were removed, a slight fall in the temperature of the arm always occurred.

Lewis and Grant<sup>6b</sup> concluded that after an increase of venous pressure a state of vasodilatation occurs of very similar grade to that produced by arterial occlusion. In none of the present experiments was the hyperemia of sufficient degree to produce hyperthermia, which always occurred after comparable periods of arterial obstruction by mechanical means.

#### CONCLUSIONS

The thermal changes following circulatory obstruction and release are comparable to those produced by the previous methods of studying these phenomena, provided certain limiting factors in the method are controlled. Mechanical obstruction results in decrement of heat, and release is followed by a hyperthermia in the limb.

Chemical obstruction of the circulation by intra-arterial injections of epinephrine is followed by a similar decrement of heat but differs from stasis produced by mechanical means in that hyperthermia does not occur after release. A preceding mechanical arrest of circulation shortens the effect of an immediately subsequent intra-arterial injection of epinephrine and leads to hyperthermia.

Injections of epinephrine hydrochloride into the femoral artery of the dog and of man in doses of 0.5 to 0.75 cc (1/1,000) produce complete vascular spasm even of the large arteries, and recovery as judged by the visual observation of hyperemic flush of the skin occurred in a centrifugal manner, beginning proximally in the thigh. Not only do the thermal curves noted after the injection of epinephrine suggest complete arrest, but amputation below the knee was accompanied by very slight hemorrhage.

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23 Rous, P., and Drury, D. R. *J. Exper. Med.* **49**: 435, 1929.

ference with the circulation due to the needling of a main artery, a tourniquet was then applied on the control leg for twenty minutes, and after its removal, 0.5 cc of a 0.9 per cent solution of sodium chloride was injected into the lumen of the control femoral artery. This did not interfere with the development of typical local hyperthermia.

In another series of five dogs, 0.5 cc of a solution of epinephrine hydrochloride (1:1,000) was injected into the femoral artery. A typical thermal curve is seen in chart 7, there occurred a steady fall of temperature in this animal for one hundred minutes, followed by a gradual rise of temperature to normal, but without hyperthermia. A rise in temperature above normal did not occur in any animal of this series.

Since the fall in temperature following the experimental injection of epinephrine resembled closely that following mechanical constriction, observations were made to determine how complete the vasoconstriction was in the latter case.

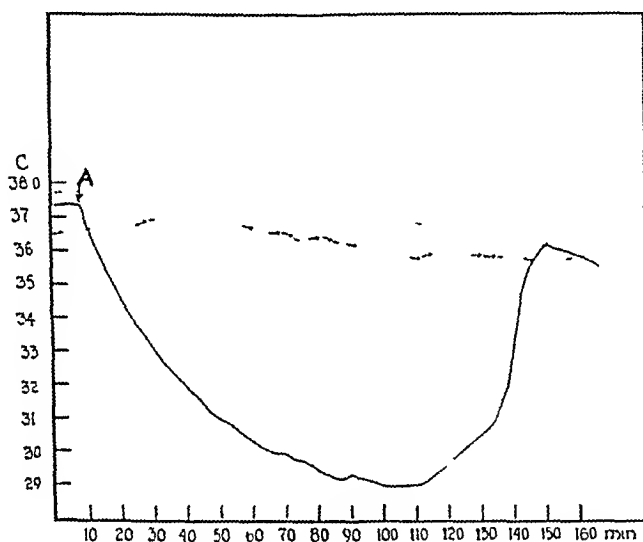


Chart 7 (dog 907)—Injection of 0.5 cc. of epinephrine hydrochloride solution (1:1,000) into the left femoral artery was followed by a gradual lowering of the temperature and then by hyperthermia. The broken line indicates the changes of temperature in the right leg, the broken line with dots indicates those in the chest wall, and the solid line indicates those in the left leg. At A, 0.5 cc of epinephrine was injected into the left femoral artery.

In four dogs weighing between 8 and 16 Kg, under ether anesthesia, a cannula was inserted in a carotid artery to obtain a record of blood pressure, and an injection of 0.5 cc of epinephrine hydrochloride (1:1,000) into the femoral artery was made. A typical experiment in a dog weighing 9 Kg follows. Three minutes subsequent to the injection, the leg was amputated just below the knee joint, without any mechanical attempt to control hemorrhage, and a vessel was held below the site of operation to collect any blood lost. Three drops of blood (0.3 cc) was lost during the procedure. The amputated portion was pale and appeared grossly to be almost completely bloodless. For two hours the stump of the leg was allowed to lie open and unsupported over the collecting vessel. There occurred a very slight ooze of blood and during this time, in all, 2 cc of



# A REVIEW OF UROLOGIC SURGERY

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## KIDNEY

*Tumors*—Wharton<sup>1</sup> contended that the outlook in the treatment of malignant tumors of the kidney is improving because of the use of radiation preoperatively to reduce the size and make nephrectomy feasible and because of the transperitoneal approach for removal

The results of lumbar nephrectomy for renal tumor have been poor because these growths, which reach enormous size, are highly vascular, are made up of friable tissue which is characteristically transplantable and have a thin, delicate capsule which is easily ruptured. The mobilization and manipulation necessary before the renal pedicle can be reached and ligated tend to produce hemorrhage, distant metastasis from milking tumor cells into the blood stream and local recurrences from rupture of the capsule. The last structure to be seen and controlled is the renal pedicle, whereas it should be the first

These disadvantages of lumbar nephrectomy are eliminated by the transperitoneal approach, which permits one to see the tumor clearly, to expose and ligate the renal vessels before it is handled or moved, to ligate aberrant vessels and the collateral venous supply, which is usually enormously enlarged, and to remove intact the kidney with the surrounding tissues, the capsule of Gerota, the perirenal fat and areolar tissue and as much of the ureter as is desired. Since these advantages

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† Deceased

1 Wharton, L R Transperitoneal Nephrectomy for Malignant Tumors of the Kidney, Surg, Gynec & Obst 60 689 (March) 1935

involving new skin the proximal hyperemic area faded and when it reached the lower part of the leg the arteries of the foot began to pulsate weakly and soon returned to normal. The process of recovery was associated with a mild tingling in the foot, much less than that experienced following the removal of a tourniquet.

In subject F N a 28 gage needle was inserted into the lumen of the femoral artery, blood was withdrawn and 0.75 cc of epinephrine hydrochloride (1:1000) was injected. Apparently the injection was made directly into the wall of the artery, because after the injection blood could not be aspirated in the syringe, and there occurred at the site of injection a pronounced systolic thrill and a loud harsh bruit, both of which persisted for one hour, then diminished and were completely absent in two hours. There were no symptoms of absorption of epinephrine as in the preceding subject.

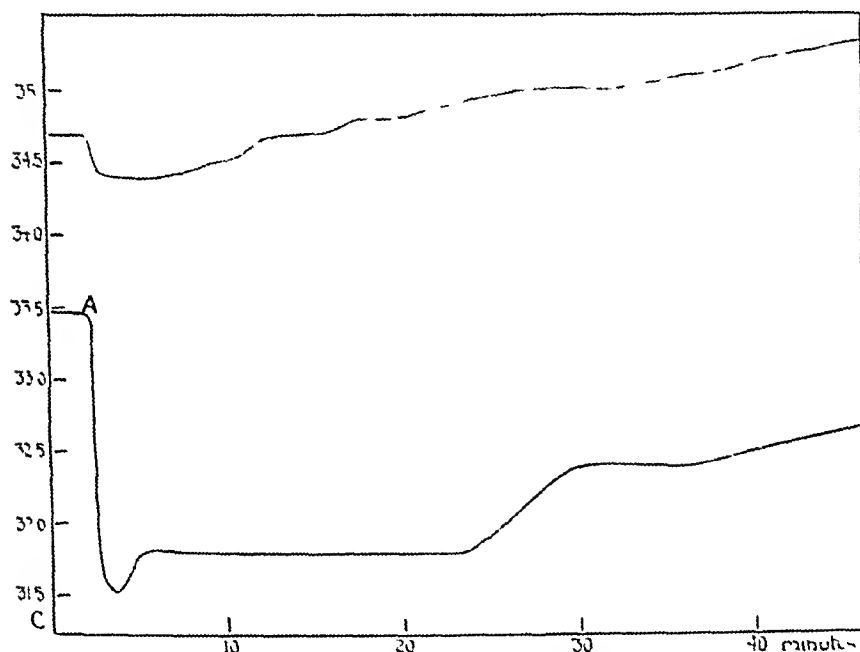


Chart 9 (subject C H) —Result of the injection of 0.5 cc of epinephrine hydrochloride into the subcutaneous tissue of the lateral part of the right thigh adjacent to the thermocouple with a similar injection of Ringer's solution into the left thigh at the same time. The time of injection is indicated at A on the chart. The upper line indicates the changes in temperature in the left thigh, and the lower line indicates those in the right thigh.

#### EXPERIMENT 5—*Local injection of epinephrine into the subcutaneous tissues*

Observations were made on three men in the following way. A thermocouple needle was inserted in the subcutaneous region of the lateral part of both thighs. After control readings of temperature were made a hypodermic needle was inserted and 0.5 cc of epinephrine hydrochloride (1:1000) was injected in such a way that the thermocouple point lay in the approximate center of the wheal produced. Into the opposite thigh 0.5 cc of Ringer's solution was injected. In each case the fluid injected was warmed to about 32°C. In each case the infiltration was accompanied by a fall in temperature much greater and of longer duration in the case of epinephrine (chart 9).

exploration the kidney and ureter appeared to be normal, and the condition was diagnosed only on examination of the specimen. Karacson expressed the belief that total nephrectomy is necessary in order to prevent recurrence. The second case was that of a man, aged 69, who had hematuria for two weeks. The ureterogram revealed in the pelvic part of the ureter a filling defect typical of tumor of the ureter. Nephrectomy was performed following which the patient recovered. Karacson called attention to the necessity of determining the condition of the remaining stump of the ureter in order to be certain that no further tumorous growth remained.

*Stone*—Brown<sup>4</sup> stated that in 1891 von Recklinghausen described certain skeletal changes, namely, marked softening of bone with deformity and multiple sarcomas, which he designated as osteitis fibrosa. In 1925 Mandl and Uebelhor resected a tumor of the parathyroid gland in a case of generalized osteitis fibrosa and observed the general and skeletal improvement that occurred. Since that time numerous observers have contributed to the knowledge of this condition. A case of hyperparathyroidism in which the symptoms were those of renal lithiasis was reported from the Mayo Clinic by Brown.

The normal excretion of calcium in the urine varies from 0.1 Gm per day in persons on a diet low in calcium to 0.5 Gm per day in those on a normal diet. Hunter and Aub and Johnson and Wilder also found that on the administration of parathyroid hormone the amount of calcium excreted in the urine was increased markedly. It is known that whatever the varying causes of the formation of stone in the urinary tract, the one definite factor is abnormal precipitation of crystalline elements normally present in the urine. Obstruction and infection may be causative factors, but probably, as has been demonstrated experimentally by Keyser, a marked increase in the normal urinary crystalloids adds so much to the burden put on the protective colloids that they are unable to perform their work efficiently, and precipitation is likely to occur. With an increased content of calcium in the tissues and in the blood stream, such as exists in cases of hyperparathyroidism, there is a marked increase of the amount of calcium in the urine, and precipitation with formation of calculi is likely to occur.

Attention has repeatedly been called to the association of hyperparathyroidism and nephrolithiasis. Castleman and Mallory observed the presence of renal stone in 20 of 25 cases of hyperparathyroidism reported from the Massachusetts General Hospital. In 11, the presenting symptoms were referable to the urinary tract, and the skeletal changes were minute or were overshadowed by the renal lesions.

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4 Brown, A. E. Hyperparathyroidism with Nephrolithiasis, Proc. Staff Meet., Mayo Clin. 10: 417 (July 3) 1935.

no case in which the circulatory arrest was produced by injection of epinephrine alone was recovery associated with hyperthermia, although this was associated with a hyperemic flush of the skin. However, in experiments in which mechanical arrest was immediately followed by constriction with epinephrine not only was the period of constriction produced by epinephrine much shorter than that in the cases in which intra-arterial injection was not preceded by the application of a tourniquet but a hyperemic hyperthermia resulted. Apparently a vasodilating substance produced by mechanical obstruction of the blood flow shortened the effect of the epinephrine.

The fact that injections of epinephrine into large arteries of the limb produce vasoconstriction in the areas supplied agrees well with observations of previous workers.<sup>22</sup> Falta and Priestley<sup>22a</sup> found that large doses of epinephrine injected into the femoral artery of dogs frequently produced no elevation of systemic blood pressure and they concluded that large amounts of this substance remained in the extremity under these circumstances. Hess<sup>22b</sup> the only previous worker who used human subjects, reported that no rise in blood pressure followed this procedure, as opposed to the results reported by Elliott and other workers on dogs. In the present experiments as opposed to those of Falta and Priestley, a rise in general systolic blood pressure was always observed in man as well as in animals. The dose used in these experiments was, however, somewhat larger than that used by Hess. Phenuster and Handy<sup>16</sup> found that the injection of small quantities of epinephrine caused a decrease in the volume of the limb in dogs. That the vasoconstriction following intra-arterial injections was complete in the present observations was suggested by the thermal curves and proved by the amputation experiments, which showed that constriction even of the large arteries of the limb, occurred. It was of interest that recovery in these experiments was slow enough that sufficient coagulation of the blood took place on the surface of the cut extremity to prevent hemorrhage after the vasospasm had disappeared. The hyperemic flush occurring in recovery, in which a circumferential band of hyperemia formed in the thigh and moved centrifugally toward the foot while the proximal areas faded indicates that spasm disappeared first in the proximal vessels and recovery occurred centrifugally. This is perhaps the explanation of the fact that a hyperthermic hyperemia did not occur following the intra-arterial injection of epinephrine, enough blood vessels were not dilated at any one time to produce an elevation of temperature. The fall in temperature caused by the local injection of epinephrine into the tissues

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22 (a) Elliott, T. R. *J. Physiol.* **32** 401, 1905. (b) Hess, O. *Arch. f. exper. Path. u. Pharmacol.* **91** 303, 1921. (c) Falta, W., and Priestley, J. G. *Berl. klin. Wchnschr.* **48** 2102, 1911.

must be considered in every case of the disease. Eleven cases are cited from a series of 23 proved cases of hyperparathyroidism at the Massachusetts General Hospital in which the presence of renal stones was the only indication of the underlying disease. A frequent finding in cases of hyperparathyroidism is the presence of many finely granular casts in the urinary sediment. The granules have been shown to contain calcium, probably calcium phosphate. The casts can be made to change into hyaline casts as the urine is made more acid by the administration of ammonium chloride by mouth. Their continuous presence in large numbers is an indication that intrarenal damage is occurring. Probably the factors governing the formation of these casts, which might be designated as microscopic calculi in the renal tubules, are the same that govern formation of stone in cases of hyperparathyroidism. These factors are the concentrations in the urine of calcium, phosphate and hydrogen ions. The formation of stone in cases of hyperparathyroidism belongs to the group wherein the predisposing abnormal factor is an excess of crystalloids in the urine.

According to Herman and Lee,<sup>8</sup> greater familiarity with the clinical picture and the biochemical problems of cystine urolithiasis has accounted for an increasing number of case reports. Cystinuria, which has an incidence of about 1/500, is predominantly a disorder of males (from 70 to 80 per cent) and is inheritable. Because of faulty metabolism of protein leading to incomplete oxidation of sulfur, cystine, a sulfur-bearing amino-acid, appears in the urine in excessive amounts usually in solution but occasionally in crystalline form. When the usual accessory factors of urolithiasis, infection or obstruction are present cystine stones are likely to form. Clinically they have a tendency to occur at an earlier age than other stones, and they are multiple and have a tendency to recur rapidly and to vary in radiopacity. At times large numbers of fairly large stones may be passed with ease because of their waxy texture.

Although the same principles that apply to the treatment of urolithiasis in general hold good for cystine stones, a more conservative attitude toward operative treatment may be adopted because (1) larger cystine stones will pass more readily than other varieties of stones, (2) there is in the absence of, and according to some writers in spite of, proper postoperative treatment, a marked tendency to rapid recurrence, and (3) in certain instances cystine stones may be dissolved by alkalis, internally and locally.

In cases of cystinuria attempts should be made to prevent the formation of stone by alkalization, which maintains the solubility of cystine

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<sup>8</sup> Herman Leon, and Lee, W. E. Cystine Nephrolithiasis, *Ann Surg* 101:746 (Feb) 1935.

Greater increments of heat occur in reactive hyperemia in the bone marrow than in the muscle of the skin in the extremity and in the limb rendered anemic before occlusion than in the congested limb

After release of constriction in the extremity there occurs a fall in the temperature of the unobstructed limbs

A method for determining the temperature of the bone marrow is presented

Greenberger, Wershub and Auerbach<sup>11</sup> attempted correlation of the incidence of renal tuberculosis in a careful study of 500 cases of pulmonary and extrapulmonary tuberculosis. Of the 500 cases in which routine necropsy was done, 252 gave evidence of tuberculous infection of the kidney. Miliary tubercles were found at 228, or 45.6 per cent, of all necropsies. These small tubercles appeared grossly as gray or yellow, single or conglomerate, the lesions often lying in rows and following the medullary rays into the renal pyramids. Microscopic examination of the sections revealed that they varied from necrotic areas to fibrotic tubercles. Tuberculous involvement of the kidneys was bilateral in 187 cases, or 82 per cent. The youngest patient was 9 months old, the oldest, 74 years, 157 were males and 71, females, 154 were of the white, 72 of the Negro and 2 of the yellow race. Only 25 per cent had urinary symptoms. The most common complaints were nocturia and frequency of urination. Destruction of the renal substance was found at necropsy in only 24 of the 500 cases, or 4.8 per cent. These statistics indicate the high incidence of renal tuberculosis secondary to advanced pulmonary tuberculosis in a large municipal sanatorium. The nondestructive, closed or miliary tuberculous lesion in the kidney was most common, the destructive, open or chronic surgical tuberculosis of the kidney is notably deficient in symptoms despite advanced renal involvement.

According to Eisendrath,<sup>12</sup> the association of renal tuberculosis and true calculous formation occurs in approximately 1.8 per cent of all cases of renal tuberculosis. Although the total number of cases is comparatively small, the possibility of such an association should be constantly borne in mind. Eisendrath reviewed 35 cases reported in the literature since 1920 and added 5 of his own. In the first place distinction must be made between the calcification which occurs in about 7 per cent of all cases of renal tuberculosis and true calculous formation. The former has definite roentgenologic characteristics, which have been described by Crenshaw. Eisendrath divided the cases of true calculi into 4 clinical groups. In the majority (26 of the 40 cases) there were stone and tuberculosis on the same side. A correct diagnosis was made in only 1 of the reported cases in this group. In the majority the stone was evident, but the tuberculosis was unsuspected. Nephrectomy is indicated. If the presence of tuberculosis is unsuspected and a less radical operation is performed, there is likely to be a persistent post-operative fistula and an early recurrence of stone.

11 Greenberger, M. E., Wershub, L. P., and Auerbach, Oscar. The Incidence of Renal Tuberculosis, *J. A. M. A.* **104**: 726 (March 2) 1935.

12 Eisendrath, D. N. Renal Tuberculosis and Nephrolithiasis as Associated Diseases, *Surg., Gynec. & Obst.* **60**: 777 (Jan.) 1935.

of transperitoneal nephrectomy are obvious, the chief reason that it has not been universally adopted is probably because of its technical difficulties and the unfamiliarity of urologists with the upper part of the abdomen

Wharton described a simple and safe operation which obviates these difficulties. Preliminary treatment, consisting of diet, rest, the administration of tonics, the control of hematuria and irradiation, is given for three or four weeks. At operation the patient is placed in the dorsal position with the back hyperextended. A long rectus incision is made, and the intestines are packed into the opposite half of the abdomen. The posterior peritoneum is incised 2.5 cm from the lateral margin of the large bowel, mobilized, and cut well above the flexure of the large intestine, it is then pushed away from the region of the renal pedicle and kidney, carrying with it the colon and the duodenum on the right side. Before the renal vessels are clamped, they should be thoroughly exposed by removal of the fat and areolar tissue by which they are concealed. After their division, aberrant vessels and the collateral venous supply are controlled, and the tumor, ureter and all of the perirenal tissue possible are removed intact. The posterior portion of the peritoneum is closed by a continuous, plain gut suture. Drainage is established by an extraperitoneal stab wound in the flank.

Priestley and Broders<sup>2</sup> reviewed 65 cases of Wilms' tumor at the Mayo Clinic. In 20 cases nephrectomy was performed, the remaining patients being treated symptomatically or by irradiation. Early symptoms are usually lacking. The method of choice in treating these patients is preoperative irradiation, followed in from three to six weeks by nephrectomy and by extensive postoperative irradiation. Of 44 patients traced up to the present time, 40 are known to be dead. No patient treated by irradiation alone is known to be living. Of the 20 patients who underwent nephrectomy, 15 are dead, 4 are living and 1 was not traced. Of the 4 patients who survived nephrectomy, only 2 have survived for any appreciable length of time (thirteen and two-tenths years and three and two-tenths years, respectively). The other 2 patients were operated on only six months ago, too recently to permit any conclusion regarding the final result.

Karácson<sup>3</sup> reported 2 cases of primary epithelial tumor of the pelvis of the kidneys and ureters. In 1 case, that of a 50 year old woman, a positive preoperative diagnosis could not be made. On surgical

<sup>2</sup> Priestley, J. T., and Broders, A. C. Wilms' Tumor, *J Urol* **33** 544 (June) 1935

<sup>3</sup> Karácson, A. V. Ueber die primären, epithelialen Geschwülste des Nierenbeckens und des Harnleiters, auf Grund von 2 Fällen, *Ztschr f urol Chir* **40** 205, 1934



the difficulty of fixing both uncut ureters into the bowel without tension, which may result in detachment later, is a decided disadvantage

In 7 cases, in 6 of which there was a single kidney, Hinman performed nephrostomy preliminary to implantation. The 6 patients with single kidneys, all of whom had intractable tuberculous cystitis, recovered. Nephrostomy was indicated in these cases of tuberculosis as a therapeutic measure in itself. After the patients improved, it was possible to determine the feasibility of uretero-intestinal implantation. However, drainage by preliminary nephrostomy should not be regarded as a stage of uretero-intestinal implantation. It complicates the problem by increasing the surgical risk, but it has its own indications.

Experience with extraperitoneal drainage after ureterotomy led Hinman to express the opinion that it might be used in conjunction with Coffey's technic 3 (transfixion-suture method), thus permitting bilateral simultaneous implantation. In the original technic only one ureter can be transplanted at a time. The ureter is exposed, opened and drained by a ureteral catheter extraperitoneally above the site of the anastomosis. This method was used in 3 cases. The result was satisfactory in the first case, in which the patient had the ureter of a single kidney transplanted to relieve an intractable tuberculous cystitis, but was unsatisfactory in the other 2 cases. The method is not recommended.

Sherman, Dinardo and Bowers<sup>15</sup> presented a new technic for simultaneous bilateral transplantation of the ureters into the rectosigmoid. A pure metallic magnesium tube is used to aid in canalization and to prevent both early and late obstruction at the site of implantation. The magnesium tube undergoes a chemical change in the presence of acid urine and slowly dissolves, it therefore requires no further attention. The results obtained in experiments on animals have been satisfactory. The immediate results obtained in man appear to warrant further use of this method.

Cabot<sup>16</sup> stated that during the past fifteen years much attention has been given to various methods of diverting the urine, all of which present some difficulty. There are three methods available at the present: nephrostomy, uretero-enterostomy and cutaneous ureterostomy.

Nephrostomy may be used as an intermediate step for drainage of the kidney when temporary diversion is indicated in cases in which rearrangement of damaged ureters is to be carried out. Cabot expressed the belief that it is rarely the best method for permanent diversion, since it is not notably more certain to preserve the integrity of the kidney and is more inconvenient than cutaneous ureterostomy. The

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15 Sherman, W. L., Dinardo, C. J., and Bowers, J. M. Ureteral Transplant Preliminary Report of a New Technique, *Am J Surg* 29:54 (July) 1935.

16 Cabot, Hugh. Diversion of Urine Above Level of Bladder, *Surg., Gynec & Obst* 61:406 (Sept) 1935.

Albright stated that renal calculi may occur in cases of hyperparathyroidism without lesions of bone and that the former may be an index of the severity of the disease and the latter an index of the duration of the disease. The importance of performing routine tests for the determination of the calcium and phosphorus content of the serum in cases of nephrolithiasis is emphasized.

Camp,<sup>5</sup> in discussing Brown's case, stated that the roentgenologic findings are interesting because they serve to emphasize the incidence of nephrolithiasis in cases of hyperparathyroidism and the assistance the roentgenologist may be in arriving at the diagnosis. The roentgenologic changes in the skeletal system in the moderately advanced stages are well established and characteristic, and the average roentgenologist should have little difficulty in making the diagnosis. However, in the early stage, in which there is a minimum of osteoporosis and in which the bones have not yet acquired the characteristic granular appearance, the diagnosis is difficult. Because of this fact the presence of generalized osteoporosis, regardless of its degree, plus associated nephrolithiasis, should lead to the exclusion of the presence of hyperparathyroidism.

Barney and Mintz<sup>6</sup> report their experience with hyperparathyroidism in relation to the formation of urinary stones. One hundred and four patients with urinary calculi were examined, a complete examination of the blood being made to determine the calcium and phosphorus content. A diagnosis of hyperparathyroidism was made in 18 of the cases. Of these, 11, or 61.1 per cent, presented not only tumor of the parathyroid gland but also urinary calculi. This makes a percentage of 10.5 persons with calculi associated with hyperparathyroidism in the group of 104 patients. The 11 patients, all having stones, together with 7 others without stones but with cystic degeneration of the bones, have all been operated on, and an adenoma of the parathyroid gland was removed. Twelve of the patients were females and 6 were males, and the ages varied from 13 to 62 years. The calcium content of the blood varied from 11.5 to 16.8 mg per hundred cubic centimeters, and the phosphorus content, from 1.4 to 4.7 mg. Barney and Mintz stated that a calcium content of the serum above 11 mg per hundred cubic centimeters and a phosphorus content below 3.5 mg should always arouse suspicion of a disease of the parathyroid gland in association with renal calculi.

Albright and Bloomberg<sup>7</sup> stated that hyperparathyroidism is a sufficiently frequent cause of the formation of renal stone that its presence

<sup>5</sup> Camp, J. D. in discussion on Brown.<sup>4</sup>

<sup>6</sup> Barney, J. D., and Mintz, E. R. Some Newer Conceptions of Urinary Stone Formation. *I. A. M. A.* **103**: 741 (Sept. 8) 1934.

<sup>7</sup> Albright, Fuller, and Bloomberg, Esther. Hyperparathyroidism and Renal Disease, *J. Urol.* **34**: 1 (July) 1935.

Calvert's range of urea concentration were ascertained. A urea content of less than 50 mg per hundred cubic centimeters was essential. If it exceeded 50 mg, operation was postponed until the patient's condition improved. When the results of these preliminary investigations were unsatisfactory, an indwelling catheter was inserted.

In only 1 of the 31 cases was a two stage operation performed, and this was done because of the patient's intolerance to an indwelling catheter. The fibrosis produced by the use of a suprapubic catheter interferes with the speed and simplicity of the major operation and the healing of the second wound. The anesthetic used in all these cases was a mixture of chloroform and ether, followed by ether given by the open drop method. Inhalation anesthetics were considered safe over such a short period as was necessary for the operation, and any risk attached to their use was not any more than that of the shock which in rare cases attended the employment of spinal anesthetics in their other operations.

The aim of the operation was speed. While the patient was being anesthetized, all possible preparations were made so that he would not be on the table more than fifteen minutes. The prostate gland was enucleated in the usual way. The hemostatic bag was inserted and distended, and a large rubber drainage tube was slipped over the abdominal end of the hemostatic bag into the bladder. The wound was then closed. No attempt was made to remove tags or to secure bleeding points in the prostatic cavity. Owing to the fact that the mortality increased in an earlier series of cases in which these methods were used, the operation was discarded. Ligation of the vas deferens was not favored, since it was considered better to allow any infection to travel to the epididymis where it did no particular harm, than to be dammed back by a ligature and start a never ending vesiculitis. The hemostatic bag used was Fullerton's modification of the Pilcher bag. It was rounded, to avoid the possibility of incontinence occurring as a result of the apex of the Pilcher bag being pulled down through the sphincter urethrae and stretching that muscle beyond the limits of recovery.

The postoperative treatment was simple. The hemostatic bag and drainage tube were left in place for forty-eight hours. The bottom of the bed was raised on blocks, and pressure was maintained on the prostatic cavity by attaching a weight of 2 pounds (0.9 Kg) to a thread which came from the interior of the bag down the urethral tube. The weight was then hung over the end of the bed. The patient usually had an uncomfortable feeling that the bladder required to be emptied while the bag was in situ, but the hemostasis obtained was excellent. At the end of twenty-four hours the fluid was removed from the bag, and

in the urine. Limitation of proteins, especially of those rich in sulfur, is a rational phase of prophylactic treatment.

*Congenital Urinary Anomalies*—Wiseman<sup>9</sup> pointed out the dangers lurking in the urinary pathway occasioned by the presence of a congenital anomaly, which may prove to be the source of obstruction and consequent urinary stasis and infection and the necessity for prompt relief in cases of such obstruction. The cases discussed exemplify the predominance of gastro-intestinal manifestations in the syndrome of obstruction of the urinary tract, in some instances to the exclusion of disturbances in the urinary tract, in other cases the gross findings in the urinary tract are normal. The applicability of plastic procedures for the relief of obstruction and the provision for drainage of hydro-nephrotic sacs have been offered as the most appropriate surgical attack, thereby preserving renal integrity, whenever the diagnosis has been made before the parenchyma is irreparably damaged.

*Tuberculosis*—Chwalla<sup>10</sup> discussed spontaneous healing of renal tuberculosis. He first gave a critical survey of the few cases of spontaneous healing of chronic renal tuberculosis that have ever been reported in the literature. He established the fact that in most of these cases there was not a real cure in the sense of scarring over of the affected area, with retention of renal function, in most of the reported cases cure was only apparent.

Chwalla reported a case which he believed was an instance of true spontaneous healing of unilateral renal tuberculosis. The patient was a 20 year old girl whose history showed a tuberculous condition. There were many typical tuberculous ulcers and granulations in the bladder, being most numerous in the region of the orifice of the left ureter, which was red and edematous. There was decreased function of the left kidney, and the urine from this side was turbid. It was impossible to catheterize the left ureter because of an impassable obstruction 1.5 cm above the orifice. *Mycobacterium tuberculosis* was found in the urine from the bladder. The right kidney was normal. At operation the left kidney was apparently not abnormal and was left in place. Two and a quarter years later the urine from the bladder was clear and free from bacilli, the return of indigo carmine was normal from both sides. Eight and ten years later, cystoscopy and inoculation of animals showed no evidence of tuberculosis. Chwalla based his assumptions on the fact that the existence of primary tuberculosis of the bladder has so far not been proved, and nothing in his case pointed to genital tuberculosis.

<sup>9</sup> Wiseman, J. L. *Congenital Urinary Anomalies*, Ann Surg 100 445 (Sept) 1934.

<sup>10</sup> Chwalla, Rudolf. Gibt es eine Spontanheilung der Nierentuberkulose? Wien klin Wchnschr 47 882 (July 13) 1934.

formed under light spinal anesthesia, several lines of lightly applied coagulation, with the use of the Stern-McCarthy resectoscope and the McCarthy roller electrode, are run over the gland in a parallel direction from the neck of the bladder forward to the region of the verumontanum. The intention is not to destroy tissue but to establish a mild reactionary inflammatory process. The lines are run at intervals, complete sealing off of the prostatic surface being avoided and allowance being made for drainage of infectious and inflammatory products. When active infection is present, suprapubic drainage is first established by a tube introduced through a large caliber trocar. In certain instances a severe infection is allowed sufficient time to correct itself before any instrumentation is attempted. An advantage attending preliminary shrinkage is that with the edematous element eliminated a clean, concise molding of the outlet of the bladder can better be accomplished.

Hambleton, Lackey and Van Duzen<sup>22</sup> made an investigation to determine whether the evolution of an explosive gas usually accompanies the use of high frequency currents in transurethral resection of the prostate gland, and, if so, at what rate the gas was evolved, its composition and how the danger of explosion might be minimized. In experiments on a series of 12 dogs there was produced in each instance a gaseous mixture which was not explosive in the absence of oxygen from external sources but became so on the addition of the proper proportion of oxygen or air. When such mixtures were exposed directly to the arc from the resection apparatus they exploded inside the bladder. The violence of the explosion was sufficient to give a loud report when it took place in the exposed bladder, but in the healthy bladders of the dogs used no ruptures were produced.

The rapid rate at which highly inflammable gases may be evolved during the use of high frequency currents for transurethral resection emphasizes the necessity of caution in order to prevent the occurrence of serious accidents. Since a small volume of gas mixed with air is sufficient to produce a violent explosion, simple lavage after each series of cuts cannot be considered an adequate safeguard unless the entrance of air is rigidly prevented. The diverse character of the gases in the mixture precludes the possibility of their removal by an absorbent. If a large amount of air or gas collects in the bladder, as shown by a large bubble, this should be aspirated by inserting a ureteral catheter into the bubble, before cutting or coagulation is done. When the patient is placed in the Trendelenburg position, the bubble is brought closer

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<sup>22</sup> Hambleton, B. F., Lackey, R. W., and Van Duzen, R. E. Explosive Gases Formed During Electrotransurethral Resections, *J. A. M. A.* **105** 645 (Aug 31) 1935.

There were 5 patients with tuberculosis on one side and stone on the other. All of them, at intervals varying from one month to one year following nephrectomy for tuberculosis, had anuria from the stone in the remaining kidney or ureter. Therefore, in a case of unilateral tuberculosis the opposite side should be examined carefully for stone. If a stone is present, it should be removed either by operative or by nonoperative methods before nephrectomy is carried out.

There were 4 patients with bilateral renal or ureteral calculi and unilateral tuberculosis. Eisendrath advised removal of the stone in the nontuberculous kidney before nephrectomy is performed on the opposite side. There are two other groups: those with bilateral renal tuberculosis and unilateral nephrolithiasis and those with bilateral renal tuberculosis and bilateral nephrolithiasis. They are of interest from the diagnostic standpoint. The treatment is that of bilateral renal tuberculosis.

*Cystic Disease*—Geisinger<sup>13</sup> discussed the nature, characteristics, clinical picture and treatment of renal cystic disease. A series of 8 cases were reported. There were 5 cases of polycystic disease, in 1 of which nephrectomy was required, and 2 cases of solitary cysts, 1 being an instance of the rare bilateral type. There was also 1 case of arteriosclerotic kidneys, with cystic degeneration in each of a type suggesting a further clinical demonstration of the operation of the Hepler theory of the origin of so-called solitary cyst of the kidney.

#### URETERAL TRANSPLANTATION

Hinman<sup>14</sup> reviewed his results in 37 cases of uretero-intestinal implantation and called attention to his modification of Coffey's technic 3. He employed the latter in 3 cases, with unsatisfactory results.

There are renewed efforts at present to improve the technic of uretero-intestinal implantation so as to prevent infection and ureteral obstruction. These efforts are directed largely to bilateral simultaneous implantation for use in adults with acquired lesions, chiefly vesical carcinoma, in whom added surgical procedures multiply the risk. Coffey's technic 2 (bilateral drainage by means of a catheter) has proved unsatisfactory because of dangers of ureteritis and suppurative nephritis from the catheters—disadvantages which were recognized by Coffey. Higgins' modification of Coffey's technic 3 and Poth's modification of Higgins' technic have the advantage of asepsis and free drainage of urine into the bladder until the anastomosis is established. However,

<sup>13</sup> Geisinger, J. F. The Cystic Kidney, *J. Urol.* **34** 202 (Sept.) 1935.

<sup>14</sup> Hinman, Frank. Uretero-Intestinal Implantation with Drainage by Extra-peritoneal Catheter, *Surg., Gynec. & Obst.* **60** 1115 (June) 1935.

In the whole group the most unsatisfactory results seem to have been obtained by resection or excision with a scalpel. The total estimated mortality in all cases in which patients were so treated was 85 per cent, as compared to a general mortality of 66 per cent. Excision or resection cannot be the operation of choice, owing to the inaccessibility of many tumors. Fulguration by the actual cautery has advantages over resection but is not so effective as cold cautery plus the radio knife. According to these statistics a combination of fulguration and excision in 287 cases carried a mortality of 52 per cent in three years, as compared to a general mortality of 66 per cent. The results in these cases were, however, much more favorable than those in which radium was used. In many instances the condition had progressed too far for fulguration, and radium was implanted. It was concluded that for the general run of carcinomas of the bladder seen by the urologist a three year cure can be expected in nearly half of the cases by this method, which is more effective than resection.

Beer<sup>24</sup> grouped growths of the bladder into three clinical and pathologic classes: benign papillomas, papillary carcinomas and solid infiltrating carcinomas, often of the squamous cell type. Further subdivision, based on microscopic data, only leads to confusion, as does the interpretation of infiltrating characteristics by the pathologist and the surgeon. A tumor may be superficial and reveal infiltration of the stalk or of the pedicle. Such a growth can be approached with some success by electrocoagulation or radium. In the infiltrating group are included growths that invade the wall of the bladder. They can frequently be felt by rectum or vagina before operation and feel, after thorough extraperitonealization of the organ, like a solid, more or less nodular plaque in the wall of the bladder. In the literature both groups appear as infiltrating, for the former, results from any form of treatment are fair, for the latter, no treatment but wide resection or total cystectomy will give satisfactory results. Seeding with radium or coagulating the really solid, infiltrating growths is a hit-or-miss procedure. Further confusion occurs in the interpretation of results by designating benign papillomas as "group 1 carcinomas" and reporting as infiltrating carcinomas those in which the involvement is superficial.

Some papillomas recur locally or in different regions after complete, well controlled destruction. In other cases papillary carcinomas or even solid growths develop years after destruction of the original growth or growths. In some cases after excision or control of solid carcinomas there are benign recurrences, although too frequently they are malignant, these are not truly recurrences but are overlooked or left-in parts of the original tumor.

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<sup>24</sup> Beer, Edwin. Surgery of Bladder Tumors, *Ann Surg* **101** 1412 (June) 1935

cases suitable for uretero-enterostomy are almost always those in which the ureters are substantially normal, the attempt to transplant abnormal ureters is likely to be followed by a higher mortality and by less satisfactory results. It is most useful in cases of congenital anomaly, certain injuries of the bladder and in a few cases of chronic interstitial cystitis. It may be employed as a preliminary to total cystectomy for cancer, but the mortality will be higher, since both ureters must be moved at the same time, and it is desirable to perform cystectomy either at the same sitting or after a brief interval. It must not be assumed on the basis of the present evidence that uretero-enterostomy enables the upper part of the urinary tract to remain entirely normal for an indefinite period, some degree of dilatation associated with infection is the rule. For patients with grossly abnormal ureters, and when the bladder has ceased to be useful, cutaneous ureterostomy has been shown to produce a lower mortality and a relatively satisfactory result. If the operation is technically well performed, and particularly if a catheter of fair size is kept permanently in the ureter up to the level of the renal pelvis, the patient is dry and comfortable and can live an effective life.

#### PROSTATE GLAND

*Hypertrophy*—Willing<sup>17</sup> discussed the treatment for prostatic hypertrophy. Between 1912 and 1932, 625 patients with hypertrophy of the prostate gland were treated in the surgical clinic at Göttingen University. Two hundred and fifty-nine patients were treated without surgical intervention, and 22 per cent of these died. Suprapubic prostatectomy was performed on 288 patients, and 16 per cent died following the operation. Perineal prostatectomy was done on 13 patients, with a mortality of 23 per cent, cystostomy was performed on 65, with a mortality of 37 per cent.

Pitlöfky-Szabo<sup>18</sup> reported the results of a study of the histologic changes in cases of hypertrophy of the prostate gland. He sectioned and examined 32 prostate glands removed surgically. Arteriosclerosis was found in 72.2 per cent and inflammatory conditions in 91 per cent. He did not consider either of these findings of etiologic importance. Basal cell metaplasia occurred in 18.2 per cent, and malignant changes occurred in 12 per cent of the cases.

Page<sup>19</sup> outlined Fullerton's method of prostatectomy and reported the results in 31 cases. Prior to operation the value for blood urea and

17 Willing, Waldemar. Ueber die Behandlung der Prostatahypertrophie, Beitr z klin Chir 159 576, 1934.

18 Pitlöfky-Szabó, Bela. Beiträge zur Histologie der Prostatahypertrophie LXII Wissenschaftliche Sitzung der Ungarischen urologischen Gesellschaft anlässlich der Ungarischen Ärzteswoche, Ztschr f urol Chir 40 210, 1934.

19 Page, W A. Prostatectomy as Performed by the Late Professor Andrew Fullerton, Brit M J 1 578 (March 23) 1935.



satisfactorily treated by cauterization through the open bladder after the method of Beer. It is Barringer's belief that tumors of grade 2 are real cancers. As far as the grade of malignancy is concerned, tumors of grade 2 and 3 can be treated either by surgical methods or by radium. Treatment of tumors of grade 4 either by radium or by surgical measures is probably inefficient, only 1 patient was cured by radium.

Tumors of the base or lateral walls of the bladder coming in proximity to the ureters or internal urethra occurred in 61 per cent of the 78 cases, in 32 per cent of the cases the tumor was on the lateral wall at the base of the bladder, back of the trigon or in the vault, and in 6 per cent the location was not given. In 165 cases from the Mayo Clinic these statistics were practically reversed, 66 per cent of the tumors occurring on the lateral walls and in the vault, and 33 per cent in the base of the bladder, trigon, urethra or orifices of the ureters. Tumors of the base are treated easily by radon seeds implanted either through the cystoscope or through the cystotomy wound. Tumors of the apex are as well treated by radium as by surgical methods, and possibly more satisfactorily by the latter method. Tumors of a diverticulum are satisfactorily treated surgically by removal of the tumor and the diverticulum. If there is secondary involvement of the bladder, radium may supplement surgical treatment. Tumors of the bladder secondary to tumors of the prostate gland are preferably treated by radon seeds implanted through the open bladder. Tumors protruding from the orifice of the ureter and secondary to tumors of the ureter are treated by surgical measures alone. If there is a secondary involvement of the bladder, implantation of radon seeds may supplement surgical treatment.

With increase in the size of the base of the tumor, radium takes ascendancy over surgical treatment, until there arrives a time when the latter is totally ineffective and radium is reasonably effective. In 78 controlled cases the base of the tumor in 21 cases (27 per cent) was between 1 and 4 sq cm, in 16 cases (20 per cent), between 4 and 6 sq cm, and in 37 cases (47 per cent), more than 6 sq cm. In 17 of the 37 cases the base was 20 sq cm and involved half or more than half of the bladder. In 4 cases the area of the base was not given. Large bulky tumors of the top of the bladder, even if they involve the ureters, are preferably treated by surgical measures.

In the first series of 109 cases there were 4 deaths in the hospital, a mortality of 3.6 per cent. In 179 cases there were 13 deaths (7.2 per cent) in the hospital. In 134 of Dean's cases in which radon seeds were implanted there were 9 deaths (6.7 per cent) in the hospital. Of 205 of Barringer's own cases 66 (32 per cent) were controlled, 50

the bed was lowered to the horizontal position. Forty-eight hours after operation the bag and drainage tube were removed.

There was 1 death in the 31 cases in which the patient was operated on by this method. Epididymo-orchitis occurred in 5 cases. With suitable treatment this cleared up in from four to seven days. Perurethral abscess was observed in 2 cases. Fistulas developed, but in both instances the fistula healed before the patients left the hospital. They were treated by suture over a catheter, after the edges of the fistula were cleaned.

*Prostatic Resection*—Caulk and Harris<sup>20</sup> stated that in using the various high frequency cutting instruments for resection of the prostate gland deeper damage to tissue is frequently produced than is desired and that to some extent it is unavoidable. High current densities applied for more than a second may do damage at depths from a few millimeters to more than a centimeter. In order that tissue may be cut with high frequency currents, an intense heat is required at the active electrode. To produce this heat it is necessary for the current to pass through the tissue from an indifferent electrode and to focalize at this point. In so doing, the paths of the current, in their concentration toward the active electrode, generate varying degrees of temperature deep within the tissue, away from the point of active burning, whereas in removal with the actual cautery approximately the same temperature is applied at the surface of the cut but no heat is produced within the tissue except by conduction from the surface.

Smith and Stockwell<sup>21</sup> stated that clinical observation and pathologic study indicated that chronic prostatitis, which obtains in the majority of cases of obstruction of this gland with attendant edema of the gland and adjacent structures of the neck of the bladder, is the underlying factor in these cases in which necrosis, sloughing and infection develop to a dangerous degree. In comparison with prostatectomy, when the element of renal or cardiac insufficiency is significant in the evaluation of mortality or morbidity risk, the hazard of resection of the prostate gland is usually confined to localized physiopathologic changes in the prostatic region.

Preliminary dehydration or shrinking of the prostate gland has been used by Smith and Stockwell in 125 cases. It reduced the morbidity, and there were no deaths in the series. Dehydration is per-

20 Caulk, J. R., and Harris, Wilbur. A Study of Comparative Effects of Various High Frequency Currents and of Thermal Cauterization in Prostatic Resection. *J. Urol.* **32**: 449 (Nov.) 1934.

21 Smith, C. K., and Stockwell, A. L. Preliminary Shrinking of the Prostate in Transurethral Resection Together with Histological Study of the Action of the Coagulating and Cutting Currents. *J. Urol.* **34**: 31 (July) 1935.

of deformity and infection of the bladder would recommend this method of treatment. In some instances these procedures may be combined with the application of radon seeds or of needles containing radium. The advantages of diathermy as a transvesical procedure for inoperable or nonresectable lesions of both high and low grades of malignancy have not been sufficiently recognized.

Quinby<sup>28</sup> stated that it is unfortunate that malignant neoplasms of the urinary bladder show a marked tendency to be situated in the base of the organ. In a recent study of 902 cases of tumors of the bladder in the Registry for Carcinoma of the Bladder, more than 75 per cent of the growths were found to originate on the trigon, on the neck of the bladder or low on the lateral wall. This means that less than a quarter of all carcinomas of the bladder are accessible to surgical removal without interference with the ureteral insertion or the vesical sphincter.

The operative removal of the urinary bladder inevitably includes the problem of diversion of the urine. There are three possible methods of disposal of the urine after the bladder has been removed. It may be delivered directly to the loin through a nephrostomy or a pyelostomy wound, each ureter may be brought out onto the abdominal wall in the inguinal or lateral regions, or the ureters may be implanted into the intestine. The disadvantage of each of the first two methods is the early and serious infection of the kidneys, besides the necessity of some sort of apparatus to collect the urine with all the attendant discomfort and complicated care. The dangers of uretero-intestinal anastomosis are the risk of immediate operative infection resulting in peritonitis and later renal involvement from obstruction to the flow of urine away from the kidney or infection or both.

At the urologic clinic of the Peter Bent Brigham Hospital it has seemed advisable not to apply one single form of treatment to cancers of the bladder but so far as possible to treat the disease in each instance by excision or radium or by partial or complete cystectomy, as seems most applicable and likely to give the best results. In those cases in which total cystectomy has been performed operability by this method has been judged on the basis of four criteria. 1 The carcinoma not only must be found to be situated in the base of the bladder but must be in such close proximity to the vesical sphincter that removal by any method must result in incontinence. 2 There should be no demonstrable metastasis of the tumor to the regional lymph nodes or to those at the aortic bifurcation. Cystectomy has not been performed in any case in which preliminary laparotomy has shown such extravesical pro-

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28 Quinby, W. C. Total Cystectomy for Cancer of the Bladder, *Ann Surg* 101:1415 (June) 1935.

to the area to be coagulated and the danger of explosion is increased as explosion does not occur unless the arc comes in direct contact with the gas

#### BLADDER

*Tumors*—O'Crowley<sup>23</sup> reported that in 902 cases of carcinoma of the bladder recorded in the Carcinoma Registry of the Urological Association, 436 growths were papillary carcinomas, 446 infiltrating carcinomas and 20 carcinomas of an unusual type. Of the 866 carcinomas that were graded, 20 per cent were of grade 1, 33 per cent of grade 2, 35 per cent of grade 3 and 12 per cent of grade 4.

The location of 854 of these tumors of the bladder, involving adjacent or multiple areas, was as follows: trigon, 32.2 per cent, lateral walls, 35.3 per cent, neck of the bladder, 9 per cent, posterior wall, 10.2 per cent, vault, 7.5 per cent, and anterior wall, 5.7 per cent. In only 473 of these cases was one area of the bladder alone involved which was as follows: trigon, 27.37 per cent, lateral walls, 41.89 per cent, neck of the bladder, 5.89 per cent, posterior wall, 10.92 per cent, vault, 7.58 per cent, and anterior wall, 6.32 per cent. Ten per cent of the cases in the Registry which were studied at necropsy showed metastasis in the following order of frequency: bones, lungs, regional lymph nodes, liver and retroperitoneal lymph nodes. Wound implantations were rare, there were none reported in this series of 902 cases. Regardless of the grade of the tumor, the percentage of recurrence varied little and followed initial treatment in 46.2 per cent of cases. Multiple tumors are more likely to recur than single growths which is probably due to the growth of new tumors. This suggests that new growth of the bladder is possibly a diffuse disease of the mucosa or possibly results from a general circulating cancerogenic substance.

The size of the tumor bears a definite relationship to the prognosis. Of 48 patients with tumors ranging from 1.9 to 2.4 cm in diameter, 54.2 per cent were alive at the end of five years. Of 91 patients with medium-sized tumors, between 2.4 and 4.9 cm in diameter, 39 per cent were alive at the end of five years, whereas of 155 with tumors larger than 5 cm, 25 per cent were alive at the end of five years. As to the mortality in the cases in the Registry according to the different grades of malignancy, at the end of five years there was a mortality of 33 per cent among 71 patients with tumors of grade 1. Among 82 with tumors of grade 2 the mortality was 60 per cent for the five year period, among 120 with tumors of grade 3, 80 per cent and among 42 with tumors of grade 4, 95.5 per cent. In this series only 102 patients are living more than five years following operation.

<sup>23</sup> O'Crowley, C. R. Carcinoma of the Bladder. *Ann Surg* 101:1407 (June) 1935.

most satisfactory method from the standpoint of functional results is uretero-enterostomy Coffey's technic 1 is probably the safest of the three methods described by him, since transplantation is carried out in two stages, cystectomy requiring a third operation The prolonged period of hospitalization is a disadvantage Coffey's technic 2, in which bilateral simultaneous transplantation with ureteral catheters is done, was used in 9 cases Three of the patients died before leaving the hospital

In an effort to eliminate the high mortality of ureteral transplantation, a less hazardous procedure has been sought A two stage method has been developed and has been employed recently in 2 cases of malignant disease of the bladder At the first stage both ureters are mobilized for a distance of 10 cm, at about the level of the pelvic brim, and are embedded between the muscularis and the mucosa of the upper part of the rectum without opening the lumen of the intestine or interrupting the continuity of the ureter Healing of this area takes place by primary union The second stage is done from fourteen to twenty-one days following the first stage The ureters are severed 2.5 cm distal to the area of implantation A purse-string suture is then laid in the wall of the intestine about the base of the severed ureter A small incision, extending into the lumen of the intestine, is made as closely as possible to the base of the stump of the ureter The end of the ureter is introduced into the lumen of the bowel and the purse-string drawn, completing the anastomosis Advantages of this method have been demonstrated experimentally There is no interruption of urinary flow at any time Primary union of the areas of first stage implantation prevents the constriction which is so commonly seen following direct implantation Ascending infections in the wall of the ureter have been noticeably absent in experimental animals

Caulk<sup>30</sup> stated that disturbances of the physiologic activities of the kidneys and ureters occur in a large proportion of cases of malignant tumor of the bladder and contribute at least 50 per cent to the mortality Early diagnosis and prompt treatment of a tumor of the bladder afford the most satisfactory protection against such involvement The tendency of the majority of these growths to be situated near the trigon, their pronounced inclination to invade and the likelihood of their causing secondary infection make the fate of the upper part of the urinary tract precarious Safeguarding the ureter is essential in the treatment of a tumor of the bladder, every precaution should be used to protect it from trauma It has been Caulk's experience that the safest and most satisfactory procedure in the treatment of this lesion of the bladder is

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30 Caulk, J R The Upper Urinary Tract in Carcinoma of the Bladder, *Ann Surg* **101** 1432 (June) 1935

Beer was of the opinion that if adequate materials are available, one should be equipped to apply all types of therapeutic methods in cases of tumors of the bladder. He was fairly certain of only two things: Benign papillomas can be destroyed and cured transurethraly or suprapubically with the high frequency current, and papillary carcinomas, infiltrating the wall of the bladder deeply, and solid infiltrating carcinomas can be completely and regularly removed only by total cystectomy. Partial cystectomy, the more extensive the better, and usually with the sacrifice of the ureter and neostomy, gives a fair result (40 per cent in three years) in cases of infiltrating papillary carcinoma, whereas the solid infiltrating growths are a more difficult problem, although partial cystectomy has resulted in cures. Radium has been used extensively in both these groups with a higher mortality than that following partial cystectomy, cure results only occasionally in cases of deeply infiltrating growths, and then only after considerable prolonged suffering.

During recent years many methods of approach have been developed in the treatment of tumors of the bladder. The approach in these cases cannot be limited to any one method, a great variety of methods should be available for use, depending on one's own experiences and on that of others. The following procedures are available: transurethral electrocoagulation with the bipolar or monopolar current, transurethral introduction of radon seeds, high voltage roentgen therapy, suprapubic cystotomy with electrocoagulation of the tumor and its base, or with electrocoagulation or excision combined with implantation of radon seeds, suprapubic, extraperitoneal resection of the involved wall of the bladder, with transplantation of the ureter or with ligation of the ureter, various combinations of the foregoing procedures for multiple tumors, resection of the main tumor and electrocoagulation or radium implantation for secondary or small tumors, and suprapubic, total cystectomy and partial prostatectomy for infiltrating malignant growths at the neck of the bladder, with transplantation of the ureters into the skin of the iliac region or with transplantation of the ureters into the colon.

Barringer<sup>25</sup> stated that the grading of tumors has been a significant aid in making a comparison of different methods of treatment possible. According to Broders' system, tumors of the bladder have been graded into four classes: grade 1, corresponding to a papilloma, and grades 2, 3 and 4, indicating increasing degrees of malignancy. Radium probably is not indicated in the treatment of papillomas, fulguration through the cystoscope or through a cystotomy wound is probably the best treatment. Extensive papilloma of the entire wall of the bladder is most

<sup>25</sup> Barringer B S. Radium Treatment of Cancer of the Bladder. *Ann Surg* 101:1425 (June) 1935.

These acquired factors, as demonstrated in his cases, are contracture of the neck of the bladder, stricture of the urethra, caruncle, hypertrophy of the trigon and polyps at the neck of the bladder. Clinically, diverticulum of the bladder of the female has no pathognomonic syndrome. It is a disease of old age. The symptoms in most cases are those of infection of the urinary tract plus obstruction. In the majority of his cases difficulty in urination did not prove to be a significant symptom as with men. The duration of the condition over a long period of years seems to be the only significant clinical fact. Differential diagnosis is to be made from false or incipient diverticulosis, a perivesical abscess with rupture into the bladder, a patent urachus or hydro-urachus, a fistulous opening to an intestinal carcinoma, hernia of the bladder or an hour-glass bladder. Treatment in most cases was directed to the causative obstructive condition.

*Cystitis Follicularis*—Hinman and Cordonnier<sup>33</sup> reported 7 cases which presented cystoscopically the picture of cystitis follicularis. The diagnosis was confirmed by biopsy in 5 cases in the series. Cystoscopy reveals that the mucosa is studded with discrete nodules of varying size, averaging about 2 mm in diameter. In some areas, particularly over the trigon and base of the bladder, the nodules are so closely packed that they appear confluent and resemble Peyer's patches in the intestine. Each nodule has a solid appearance in contrast to the more translucent character of the cysts in cases of cystitis cystica. There is a generalized capillary injection of the mucous membrane, such as is observed in cases of chronic cystitis. Microscopically, each nodule is composed of a solitary lymph follicle with densely packed lymphocytes at the periphery and a typical germinal center. Clinically, there are no distinguishing symptoms. They are those of chronic inflammation of the bladder. At times the patient is entirely without symptoms, and still the mucosa of the bladder is found to be covered with these nodules. All of the patients in this series had recurrent attacks of dysuria, such as frequency, burning, urgency and nocturia. Cystitis follicularis must be differentiated from cystitis cystica, cystitis glandularis, cystitis granulosa, cystitis emphysematosa and bullous edema.

*Ulcer*—Lazarus<sup>34</sup> stated that simple chronic ulcer of the urinary bladder is a distinct clinical entity, the etiology of which is unknown. The lesion, while usually solitary, may occur in more than one place. The site of predilection is the trigon, particularly the region about the orifices of the ureters. The significant symptoms are dysuria, fre-

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<sup>33</sup> Hinman, Frank, and Cordonnier, Justin. Cystitis Follicularis, *J Urol* **34** 302 (Oct) 1935.

<sup>34</sup> Lazarus, J. A. Simple Chronic Ulcers of the Urinary Bladder. Report of an Unusual Case, *J Urol* **34** 111 (Aug) 1935.

(24.3 per cent) of the patients were well after three years and 44 (21.4 per cent) after five years

Implants of radon seeds are peculiarly applicable in controlling tumors of the bladder, but this is not true of the radium element in needles. There is almost always a single plane, about 1 cm deep, to irradiate, and needles are too awkward and large to irradiate such a plane effectively. Radium needles, moreover, have to be removed, while radon seeds do not, and there is a possibility that radium needles will be displaced during the process of the treatment.

Dean<sup>26</sup> stated that the average successful dose of radiation for treating tumors of the bladder is about from 7 to 10 skin erythema doses within sixteen days. The 4 Gm radium pack is not suitable for treating this lesion because of the time required to administer a satisfactory dose. The 200 kilovolt unit can furnish about 50 per cent of the required dose. Therefore, it offers slight hope of curing a tumor of the bladder, and even its palliative value is questionable. The 700 kilovolt unit can so closely approximate the required dosage that one is justified in employing it in the treatment of cancer of the bladder. It is assumed that a complete urologic examination has been made in all cases and that the choice of treatment has been made by the urologist.

Counseller and Braasch<sup>27</sup> stated that the use of diathermy in the surgical management of carcinoma of the bladder is gradually being extended, for it has brought cases in which the condition formerly would have been regarded as inoperable, or the growth as nonresectable, within the field of successful treatment. Seventeen patients whose conditions were considered inoperable were treated extensively with diathermy alone, and 15 of the 17 (88 per cent) lived more than five years. Two others have recently died from unrelated conditions. Tumors of the bladder that are comparatively small and are of a malignancy of grade 1 or 2 are usually controlled by transurethral electrocoagulation. Some of the early, circumscribed lesions which are graded 3 or 4 and which can be seen easily and give no clinical evidence of infiltration may be treated similarly. The more extensive, highly malignant lesions and the widespread lesions with low degrees of malignancy are attacked preferably by the suprapubic route. Whenever the lesion can be completely removed surgically, by either segmental resection or excision, this is the operation of choice. Electrocoagulation is used for the inoperable lesions, of both high and low grades of malignancy, confined to the base. The small number of recurrences and the lack

<sup>26</sup> Dean, A. L., Jr. Treatment of Bladder Cancer with External Irradiation, *Ann Surg* **101** 1428 (June) 1935.

<sup>27</sup> Counseller, V. S., and Braasch, W. F. Diathermy for Carcinoma of the Bladder, *Ann Surg* **101** 1418 (June) 1935.



position of the opening, its size, the amount of cicatricial tissue that surrounds it and whether or not malignant disease is present. The following types of operations were used in this series of cases: repair of the fistula by the transvesical approach (8 cases) and by the vaginal approach (28), ureteral transplantation into the intestines (10) and into the bladder (3) and nephrectomy (3). There was no treatment in 19 cases.

Cullen<sup>37</sup> stated that when a vesicovaginal fistula is high and the vagina narrow, closure may be difficult. If Schuchardt's incision is made, the fistula comes clearly into view and may be more readily closed. If sufficient exposure cannot be obtained by one incision of this type, it may be necessary to make a similar one on the opposite side of the vagina. In rare cases in which the greater part of the base of the bladder is missing and in which one orifice of the ureter opens on the margin of the fistula, it may be difficult to make a satisfactory closure of the fistula. Free mobilization of the bladder is essential. Owing to the fact that the ureter runs obliquely in the wall of the bladder for more than 1 cm., it can be slit at least 1 cm. Its opening into the bladder is then well removed from the edge of the fistula, which can be satisfactorily closed. Fistula following complete hysterectomy for cancer of the cervix formerly occurred rather frequently. After removing the uterus, Cullen sutures the peritoneum of the bladder to the cut edge of the anterior wall of the vagina. After this procedure, when the bladder distends it is only the peritoneally covered portion that dilates. The base of the bladder, where fistula is prone to develop, remains contracted and is well protected. In Cullen's cases the number of postoperative fistulas has been markedly decreased by this simple method. In many complicated cases of myoma it has been necessary to dissect out one or both ureters to ascertain whether they have been injured, at which time any damage can be immediately corrected.

Miller<sup>38</sup> stated that the popularity of transplantation of the ureters may tend to do away with more conservative measures in the management of vesicovaginal fistulas. The success of closure of this lesion depends on wide separation of the bladder and vaginal wall and independent closure of these two layers. In some cases in which the fistula is unusually large, the bladder has been closed without any attempt to coapt the vaginal area. If there is extensive destruction, separation of the two layers should be sufficiently wide to permit closure of the lesion of the bladder without tension, no sutures should be placed in

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37 Cullen, T. S. Discussion on Vesicovaginal Fistula, *Am J Surg* 28 265 (May) 1935.

38 Miller, C. J. Discussion on Vesicovaginal Fistula, *Am J Surg* 28 269 (May) 1935.

gression of the malignancy 3 Renal function must be normal in at least one kidney, but preferably in both, as demonstrated by ureteral catheter 4 Actively growing carcinoma must be demonstrated on microscopic examination

All patients are first studied by cystoscopy and by roentgenologic examination of the chest and skeleton to exclude a diagnosis of metastasis Renal function is estimated, and pyelograms are made, retrograde pyelograms are made if possible, and if not, intravenous ones At the first operation the region of lymphatic drainage away from the bladder is investigated, and if no secondary deposits of malignant tissue can be determined, anastomosis of a single ureter is performed Following recovery from this operation, the second ureter is transplanted, and the bladder, together with the prostate gland of the male, or of the whole urethra of the female, is excised The electrosurgical needle is of advantage in the conduct of the anastomoses as well as in the excision of the bladder Ten patients to date have been treated in this manner Two are alive, one is a woman who for three years has been without evident recurrence, and the other is a man who in the eight years following treatment has had recurrence about the rectum and prostate gland during the past year Of the remaining 8 patients, 2 died as a direct result of an early form of the operation, which was imperfect in some way The remaining 6 have died of recurrent cancer at longer or shorter periods after operation In none of these cases, however, was there any further acute difficulty in the urinary tract

Nesbit<sup>29</sup> stated that cystectomy for malignant growths of the bladder is indicated in cases in which there is such involvement of the trigon that the orifices of the ureters cannot be spared when destructive methods of treatment are used, in cases of infiltrative involvement of the outlet of the bladder so that adequate attack locally is destructive to the sphincters, in cases of multiple infiltrative tumors and in cases in which the neoplasms are of a low grade of malignancy but have a marked tendency to recur and spread in spite of conservative treatment and eventually become penetrative or highly malignant

There are three methods of disposing of the urine following cystectomy Drainage of the kidney by nephrostomy or pyelostomy has disadvantages that contraindicate its use if other methods can be utilized Cutaneous ureterostomy has long been considered a safer method than uretero-intestinal anastomosis The drainage tubes and apparatus necessary following the latter procedure are difficult to manage and can rarely be fitted sufficiently well to prevent some leakage of urine The

29 Nesbit, R M Total Cystectomy and Ureteral Transplantations in Malignant Conditions of the Bladder with a Description of a New Operative Procedure, *J A M A* 105 852 (Sept 14) 1935

is usually tightly contracted during ejaculation. Instances are cited in which the internal sphincter is paralyzed or injured after operation in cases of prostatic hypertrophy and of certain nervous diseases. Two cases are reported of direct injury to this localized region, with the result in all cases that ejaculation failed. In cases of hypertrophy of the prostate gland the internal sphincter is dilated by the growing adenoma, and at operation it is further stretched and perhaps cut across. Continence then depends on the external sphincter. Two cases are reported in which the external sphincter had previously been paralyzed, total incontinence resulting.

In disease of the central nervous system dilatation of the internal sphincter resulting in funnel-neck is common. A series of patients with disease of the nervous system were examined in order to determine the frequency of this sign. Other cases were reported in which it occurred independent of any nervous condition.

The part the sphincters play in ejaculation is discussed and illustrated by reports of further cases of paralysis of the sphincters. In the normal way the external sphincter weakens during coitus, especially during ejaculation, but when the internal sphincter is paralyzed no weakening is evident. Penile erection is associated with spasm of the internal sphincter, and spasm of the internal sphincter produced by irritation, such as stone in the bladder, may produce priapism. The varying types of adenoma bear different relationships to the internal sphincter. The view that submucosal glands give rise to enlargement of the prostate is supported. The influence of enlargement of this gland on the internal sphincter is discussed.

*Cystometry*—Watts and Uhle<sup>41</sup> presented evidence of representation of the bladder in the cerebral cortex and the region of the hypothalamus and even more caudal in the brain stem. The nature of the evidence indicated that representation for this viscus contains both excitatory and inhibitory units. Eleven patients with tumor of the brain associated with neurogenic bladder were studied. Patients with hypertonic curves gave histories of urgency and periodic involuntary urination. Two patients with hypotonic curves had difficult urination, followed by retention requiring catheterization. The other patients with this type of curve had no urinary symptoms. The abnormalities of function, tone and sensation of the bladder of patients with tumor of the brain are probably the result of a disturbance of representation of the bladder in certain parts of the brain or of tracts descending from them.

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<sup>41</sup> Watts, J. W., and Uhle, C. A. W. Bladder Dysfunction in Cases of Brain Tumor. A Cystometric Study, *J. Urol.* **34** 10 (July) 1935.

the application of radon seeds and coagulation, either suprapubically or, preferably, endovesically. Occasionally an erosive destructive tumor which implicates the ureter requires resection with reimplantation. In many cases such a tumor may be satisfactorily treated by intravesical implantation, the orifices of the ureters being guarded by an indwelling catheter. Reimplantation of the ureter in the hands of the average surgeon is fatal to the kidney. In cases of generalized carcinomatous change throughout the vesical cavity, actual cauterization, with or without the implantation of radon seeds, occasionally yields satisfactory results. Total cystectomy has a limited field, when performed, it demands preliminary ureteral drainage, preferably through an iliac-cutaneous implant, and rarely preliminary uretero-intestinal anastomosis. Ureterostomy or nephrostomy is occasionally necessary as a palliative measure to relieve suffering and to prolong life.

*Diverticulum*—Melen<sup>31</sup> discussed the various surgical procedures for treating diverticula of the bladder and described a lateral approach through a pararectus or modified Gibson incision. This facilitates exposure, especially when the diverticulum is on the side or at the inferolateral angle, and it permits its extravesical removal without opening the bladder. A pararectus incision is made from the umbilicus to 2.5 cm above Poupart's ligament and is then continued at a right angle to the midline. This gives much more room than through the standard midline incision, permits sharp dissection if there is peridiverticulitis and facilitates identification and isolation of the ureter several inches above the diverticulum.

The bladder is not opened in the midline as in the usual combined extravesical and intravesical method. The diverticulum is freed by blunt and sharp dissection and is severed from the bladder. The opening is then closed from the outside after a tube is inserted through it for drainage. This does away with another artificial opening into the bladder. It is, of course, imperative to remove whatever obstruction may exist at the vesical neck before excision of the diverticulum is planned. This can usually be done transurethrally. The advantages and disadvantages of the various methods of diverticulectomy are discussed.

Kutzmann<sup>32</sup> stated that diverticulum of the urinary bladder of the female occurs rarely. This lesion is the result of both congenital and acquired anatomic factors. Diverticula form less frequently in women since there are fewer acquired obstructive factors of sufficient severity.

<sup>31</sup> Melen D. R. Lateral Approach for Operating upon Diverticula of the Bladder, *Surg., Gynec. & Obst.* 61:184 (Aug.) 1935.

<sup>32</sup> Kutzmann A. A. Diverticulum of the Urinary Bladder in Women, *Am J. Surg.* 29:102 (July) 1935.

advantage of the hormonal test in the control of treatment is shown in Hinman's cases. Patients who do not have metastasis fail to excrete the hormone within two weeks after castration. When the hormone persists, though reduced in quantity, metastasis has probably occurred even though it cannot be demonstrated clinically. The third step is the consideration of radiosensitivity. This can be predicted by past experience with similar tumors and clinically tested by watching the effect of irradiation on metastasis, when present, and on the amount of hormone in the urine. The determination of this sensitivity may be called the therapeutic test of irradiation. From 3,000 to 4,000 roentgen units to each field, requiring a period of three weeks for administration, will show by the effect clinically on metastasis, and biologically on the amount of hormone excreted one to two weeks later the relative degree of radiosensitivity.

On the basis of the foregoing considerations patients may be divided into two groups. Group 1 contains those patients without clinical evidence of metastasis who are in good physical condition, these can be subdivided, by the result of a hormonal test two weeks after castration, into a negative and a positive subgroup. The negative subgroup includes the few patients cured by castration. All of these patients should, however, receive a hormonal test every three to six months for two years or longer. Reappearance of the hormone in the urine indicates metastasis. Should the microscopic structure of the tumor be similar to that which experience has shown is highly radioresistant early radical removal of the preaortic lymph zone should be considered, regardless of the effect of castration on the hormone. The disappearance of the hormone after castration is only relative evidence of cure for metastasis may not produce sufficient hormone in the urine to give a reaction. Group 2 contains patients with clinical evidence of metastasis. Castration may be indicated for local relief but is done mainly for diagnosis. Experience has shown that these patients are inoperable and that irradiation is the only curative treatment. The prognosis depends on the extent and rapidity of metastasis and the general physical condition of the patient as well as on the type of tumor and its radiosensitivity.

A fairly accurate forecast of the probable course in any given case is possible by these studies. The chance of recovery may be estimated as good, fair or poor. The prognosis is good when the patient is physically fit there is no demonstrable metastasis and the hormone has disappeared from the urine. The patient's condition is considered as fair when he is in good physical condition and the structure of the tumor indicates that it will respond well to roentgen therapy, however, metastasis has appeared, and the hormone has persisted, even though it appeared to be diminishing under irradiation. A poor outcome is

quency and hematuria. The kidneys are never affected. Calcification occurs in a later stage of the life cycle of this ulcer, so when one is seen early encrustation is not present. Generally, the capacity of the bladder is not reduced. The diagnosis is made by excluding any of the usual causes of ulcer of the bladder such as tuberculosis, syphilis and neoplasm. The prognosis in cases of simple chronic ulcer is favorable. Treatment has consisted of the application of silver nitrate, scraping of the ulcers or excision. Lazarus did not obtain satisfactory results with these methods but did obtain a complete cure by the intravenous injection of neoarsphenamine.

*Bilharziasis*—Loeweneck,<sup>35</sup> in discussing schistosomiasis, stated that cystoscopy in cases of bilharziasis furnishes the most data if performed a few days after treatment has been instituted. The Morgenstern cystoscope is the most satisfactory instrument to use in examining, checking and treating this condition. Simple urinalysis is of small value in determining whether the condition is still present, cystoscopic examination is usually necessary. The disappearance of eosinophilia is the most decisive evidence of a cure.

*Vesicovaginal Fistula*—Lower<sup>36</sup> stated that vesicovaginal fistula is regarded as an extremely rare condition but that in spite of improved surgical and obstetric technic there is still a considerable number of women who present themselves for treatment of this lesion. It may result following childbirth or from a surgical accident during a pelvic operation, or it may result from a malignant condition of the bladder or cervix, from the application of radium in the treatment of a malignant process in the pelvis or from the invasion of the malignant growth itself. Fistula developed in a series of 71 cases reported by Lower as follows: as a result of childbirth in 10 cases in which cancer was not present and as a result of operative trauma in 32, and in cases in which cancer was present, as a result of operative trauma in 11, radium treatment in 13 and invasion by cancer which had not been treated in 5.

Treatment of this lesion must be individualized, for no one type of operation or approach can be used satisfactorily in all cases. In many of the cases observed by Lower repeated unsuccessful attempts have been made to close the fistula. In 1 case an attempt at repair had been made eleven times. Each effort at treatment is made more difficult by the presence around the opening of hard fixed scar tissue. The choice of the method in treating this condition depends on the

<sup>35</sup> Loeweneck, M. Zur Behandlung der Schistosomiasis haematobium, *Ztschr f urol Chr* 40 202, 1934.

<sup>36</sup> Lower, W. E. The Treatment of Vesicovaginal and Ureterovaginal Fistula. *Am J Surg* 28 234 (May) 1935.

gland when infection is present, and it occurs in cases of infections of the genito-urinary system in general. The important facts in the diagnosis of suppurative orchitis are persistent fever, leukocytosis, progressive swelling, pain and tenderness of the testis and local fluctuation. Early diagnosis of abscess of the testis makes possible the saving of testicular tissue by prompt incision and drainage.

Rosenberg<sup>45</sup> reported 6 cases of abscess of the testis and 1 case of necrosis of the testis. Four of the abscesses were associated with gonorrhea and a complicating epididymitis, in 2 cases the condition was due to chronic infection of the urinary tract by nonspecific epididymitis. The necrosis was probably due to torsion of the spermatic cord following violent muscular effort. Abscess of this organ is usually due to some infection either in the urinary or in the genital tract, excluding instances in which it is associated with typhoid, influenza, cellulitis and osteomyelitis. In the last-named condition, involvement of the testis is probably of hematogenous origin.

Generally there are four types of abscess of the testis. Abscesses associated with gonorrhea and a complicating epididymitis are usually small, and the testis generally sloughs out in its entirety. Abscesses associated with chronic infection of the urinary tract or genital tract are usually large and cause complete destruction of the testis. They occur in such conditions as obstruction of the prostate gland when drainage by a catheter has been instituted and urethral instrumentation has been employed. The third type is associated with torsion of the spermatic cord. The fourth type is associated with systemic infections, such as typhoid, variola, influenza and cellulitis, and is usually a true orchitis and rarely leads to suppuration. When testicular abscesses occur in this instance, they are probably due to phlebitis of the spermatic vessels. Abscess of the testis associated with tuberculosis or a malignant condition is not considered. Abscess of the testis usually results in complete destruction of the organ, whether or not drainage is instituted. Early diagnosis is essential in order to conserve as much testicular tissue as possible.

*Undescended Testis*—Webster,<sup>46</sup> who treated 11 patients who had undescended testes with an extract of the urine of pregnant women, stated that in 10 of the cases the testes descended into the scrotum during treatment. The 1 case in which failure occurred was that of a man 26 years of age who had undergone previous exploration of the inguinal canal, the purpose being to locate the organ. In all of 3 cases of bilateral undescended testis, descent into the scrotum occurred. In 2

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45 Rosenberg, William. Abscess of the Testicle, *J Urol* **34** 44 (July) 1935

46 Webster, Bruce. Effect of Anterior Pituitary-Like Principle from the Urine of Pregnancy on Undescended Testes in Man, *J A M A* **104** 2157 (June 15) 1935

the vaginal layer. Another feature is to separate the uterus from the bladder, even to the extent of opening the peritoneal sac, making a wide separation of the bladder from the broad ligaments above. This facilitates closure of extensive lesions with satisfactory results.

*Atony*—Braasch and Thompson<sup>39</sup> stated that atony of the bladder is never primary, it is caused by abnormal innervation, by obstruction or by both. Continuous retention of urine from any cause will produce atony of the vesical wall. In some cases it may be difficult to determine which factor is involved. In most cases of atony, obstruction, either primary or secondary, is the predominating factor. The factors involving sphincteric dysfunction are imbalance of innervation, with predominance of the sympathetic or filling nerves, rigidity, or failure of adequate relaxation of the internal sphincter, referred to as "dysectasia," and apparent failure of coordination of reflexes involved in the act of urination centering in the vesical neck, to which the term achalasia has been given. The first condition can be favorably influenced by presacral neurectomy, and the second usually can be remedied by thorough transurethral resection. The abnormal tissue, which interferes with the function of the neck of the bladder, may in some cases be overlooked. It is necessary to remove such tissues completely and to free every cicatricial contraction in order to restore sphincteric function. Sphincteric abnormality in the female presents problems quite different from those offered by corresponding conditions in the male. In most cases judicious removal of sphincteric tissue will overcome retention but subsequent presacral neurectomy may be necessary. Localized or partial atony may follow destruction of branches of the pelvic nerves in the course of an operation on the bladder. Various other types of atony may occur.

With acute retention, such as frequently occurs following an abdominal operation, the advisability of drainage of the bladder before it becomes overdistended should be emphasized. In contrast, with retention following extensive injury to the spine, overflow of the bladder should be permitted rather than catheterization.

*Musculature of Vesical Neck*—Macalpine<sup>40</sup> stated that two muscles, one voluntary and the other involuntary, and an inch or more apart, exist at the neck of the bladder, both functioning as sphincters. This dual musculature is explained by the emergence of the ejaculatory ducts between them. If both of these muscles are open when semen is discharged, secretion may escape into the bladder or to the exterior, also any urine in the bladder will flow out. The internal sphincter

39 Braasch, W. F. and Thompson, G. J. Treatment of the Atonic Bladder, Surg, Gynec & Obst 61 379 (Sept) 1935

40 Macalpine, I. B. The Musculature of the Bladder Neck of the Male in Health and Disease, Proc Roy Soc Med (Sect Urol) 28 39 (Nov) 1934



layers are deposited. If the condition is not treated, obstruction of urine of severe degree will develop, which without intervention may give rise to the formation of a fistula. Chronic irritation has caused the development of cancer of the glans penis in at least one instance, and pressure atrophy of the glans is common. Diagnosis rests on the realization of the existence of such a condition, and the treatment, without exception, is circumcision.

*Tumor of Cowper's Gland*—Uhle and Archer<sup>48</sup> stated that primary carcinoma of Cowper's gland is exceedingly rare. Only 4 cases were found in the literature of the various countries of the world. The etiology of this lesion is obscure. Uhle and Archer reported a case in which they considered themselves warranted in identifying the tissue as adenocarcinoma arising primarily from Cowper's gland. The alveolar spaces were numerous and were lined with small cells of pyriform type in which mucous-secreting elements were evident. Hyperplasia of the intra-acinar type was definite. These hyperplastic acini showed wide variation in size, in some areas the acini were represented by small islands of epithelial cells with no definite arrangement and appeared to lack a basement membrane.

Symptoms in cases of malignancy of Cowper's gland are primarily in the perineum and rectum. Persistent local discomfort, aggravated by sitting or walking, and pain on defecation are the most common symptoms. If frequency, urgency, dysuria and burning are also present, the lesion has probably extended to the urethra or periurethral tissue. If urinary difficulties are the predominating symptoms, the diagnosis of primary carcinoma of the urethra is more probable. Sometimes the chief complaint is that of a lump or swelling in front of the anus. Tenderness may or may not be present. The skin of the perineum may or may not be fixed. The proximity of the neoplasm to the rectal wall often leads to a mistaken diagnosis of a rectal lesion. The patient in the case herein reported was treated for an anal fistula, the mucosa of the rectum was fixed to the mass while the boundaries of the infiltrative tissue were difficult to discern both by perineal and by rectal examination.

The treatment of carcinoma of Cowper's gland is surgical. Early diagnoses have been rare, most patients have been seen in the end-stages, when only a portion of the tumor could be excised, so that a remnant had to be left to be treated by palliative measures. With the addition of roentgen and radium therapy, more satisfactory results may be expected in the future.

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<sup>48</sup> Uhle, C. A. W., and Archer, G. F. Primary Carcinoma of Cowper's Gland. Report of a Case with a Review of the Literature, *J. Urol.* **34** 128 (Aug.) 1935.

## TESTES

*Tumor*—Hinman and Powell<sup>42</sup> stated that tumor of the pituitary gland, embryonal tumor and pregnancy are known causes of the appearance in the urine of gonad-stimulating hormones. The stimulation of growth of the gonads and genitals of infantile animals varies with the origin of the hormone producing it, the amount present in the urine and the animal used for the injections. Infantile mice and rats are used. A qualitative test for as low as 250 units is made first on fresh, unaltered morning urine. If the reaction is positive, a quantitative test can be made. The microscopic ripening of graafian follicles is more easily observed in mice than in rats, and the gross enlargement of the uterine horns is more definite and diagnostic in mice than in rats.

The majority of tumors of the testes are embryonal, and the urine of patients with such a tumor contains a substance which produces gross enlargement of the uterine horns or microscopic ripening of ovarian follicles when injected into infantile female mice and rats. The presence of such a gonadotropic hormone in the urine of a patient with a tumor of the testis is presumptive evidence of malignancy of the testis, and its absence is strong but not definite evidence against the presence of a malignant condition. The effect of irradiation on the amount of hormone in the urine, as determined by quantitative methods before and after irradiation, gives a good indication of radiosensitivity, and it may be used as a therapeutic test in conjunction with the clinical effect on metastasis, when present. The therapeutic test of irradiation must be interpreted in conjunction with the histologic structure of the tumor, the clinical absence of metastasis or the character of metastasis when present and the physical condition of the patient. The hormonal test, correlated as before mentioned, permits more accurate prognosis and better control of treatment than has been possible heretofore and it may be of value in the classification of tumors the nature of which is questionable on histologic study alone.

Hinman<sup>43</sup> stated that the prognosis and treatment of a tumor of the testis may be determined by the following three considerations and lines of procedure. Early and definite diagnosis is the first step in the treatment of the disease. The hormonal test, in the short period of its application, seems to indicate with accuracy the presence or absence of a testicular malignant process. The second step is the determination of the presence or absence of metastasis by clinical examination and biologic test. For practical purposes, patients can be divided into two groups: those without metastasis and those with metastasis. The

42 Hinman, Frank, and Powell, T. O. The Gonadotropic Hormone in the Urine of Men with Tumor of the Testis. *J Urol* **34** 55 (July) 1935.

43 Hinman, Frank. The Prognosis and Treatment of Tumors of the Testis. *J Urol* **34** 72 (July) 1935.

for the control of this disease, with varying results. In 1927 Pieri<sup>5</sup> performed unilateral resection of the splanchnic nerves for intestinal atony, and recently de Takats and his associates, on an experimental basis,<sup>6</sup> recommended bilateral resection of these nerves for the relief of juvenile diabetes.

In evaluating the effects of this surgical procedure, the primary interest of most investigators has been directed to subsequent manifestations of clinical improvement. These have been variable, owing perhaps, to the extent and duration of the underlying disease. However, unilateral and bilateral resection of the splanchnic nerves have made available opportunities for investigating the specific functions of these nerves and their rôle in the body economy.

Many concepts regarding the physiology of the human splanchnic nerves have been derived from experimentation on animals. Some views, not entirely accurate, have persisted for many years without challenge. Thus, the investigations of Bayliss and Starling<sup>7</sup> in 1899 indicated that the splanchnic nerves exert a tonic inhibitory influence on intestinal movement. At no time did they obtain evidence that these nerves possess a motor function. Subsequent experimentation has altered this view.<sup>8</sup> More accurate information regarding the manifold function of the human splanchnic nerves will be available when direct observations are made on man. This is now possible owing to the frequency with which resection of the splanchnic nerves is being employed in the management of various diseases.

Recently an opportunity for studying objectively one function of the splanchnic nerves—namely, their influence on the human gastric motor mechanism—became possible when bilateral resection of the splanchnic nerves was accomplished for the control of severe diabetes.<sup>6</sup> A review of the literature has failed to reveal any reference to another study of this kind. The purpose of this paper is to report the results of our observations.

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5 Pieri, Gino. La resezione dei nervi splanchnici, *Ann. ital. di chir.* 6: 678 (July) 1927, quoted by Craig and Brown.<sup>3</sup>

6 (a) de Takats, Geza, and Cuthbert, F. P. Surgical Attempts at Increasing Sugar Tolerance, *Arch. Surg.* 26: 750 (May) 1933. (b) de Takats, Geza, and Fenn, G. K. Bilateral Splanchnic Nerve Section in a Juvenile Diabetic, *Ann. Int. Med.* 7: 422 (Oct.) 1933. (c) de Takats, Geza, Fenn, G. K., and Trump, Ruth A. Splanchnic Nerve Section in Juvenile Diabetes, *ibid.* 7: 1201 (April) 1934.

7 Bayliss, W. M., and Starling, E. H. The Movements and Innervation of the Small Intestine, *J. Physiol.* 24: 99, 1899.

8 Barry, D. T. The Functions of the Great Splanchnic Nerves, *J. Physiol.* 75: 480, 1932.

expected when the patient loses ground physically, when metastasis resists treatment or recurs rapidly and when the amount of hormone in the urine is only slightly affected or even increases

Of 25 patients with no evidence of metastasis, 14 underwent radical operation, 9 for tumor on the right side and 5 for tumor on the left side. Ten were living at the time of the report, all with a good prognosis. 4 were dead. Seven showed metastasis in the glands removed at operation, 4 of these patients were living, after fourteen years, four years and ten months, one year and one month and three months, respectively. Three are dead. Seven had glands removed which did not show metastasis, in 2 of these patients there was an unusual degree of endothelial hyperplasia, and 1 was living and well after six years and one month and the other was dead. The 5 remaining patients were still living after eight years and nine months, two years and eight months, one year and four months and one year (2), respectively.

Of the 11 patients without metastasis treated by castration and roentgen rays, 8 were living. 1 after two years, with a good prognosis, 4 with only a fair result because the hormonal tests gave positive results, and 3 with a definitely poor prognosis. Of the 4 patients with a fair prognosis, 1 lived seven years before metastasis appeared, but the amount of hormone in the urine was increasing in spite of roentgen therapy, another lived seven years since castration but although metastasis was not evident clinically, the amount of the hormone in the urine was increasing and the other 2, with a fair prognosis, had lived one and three years, respectively, without clinical evidence of metastasis but with positive reactions to hormonal tests. Of 29 patients with clinical evidence of metastasis when first seen, only 10 were alive + with a fair prognosis.

*Infection*—Mathe<sup>44</sup> reported a case of the fulminating type of testicular abscess, due to the colon bacillus, affecting a young man with nongonorrheal infection of the genito-urinary tract. It followed instrumentation, a differential diagnosis was difficult to make, and the condition was relieved by orchidectomy.

Suppurative orchitis is relatively infrequent compared to epididymitis, epididymo-orchitis and orchitis, but it is not a rare disease. The possibility of its presence should be considered when acute inflammatory processes of the testis are being dealt with. Infection of the testis takes place through the blood stream, lymph channels and natural channels by way of the vas deferens and may be due to torsion of the spermatic cord, to trauma to the testis during operation or to toxic poisoning. It is a complication of gonorrheal and nongonorrheal urethritis. It may follow catheterization or operation on the prostate.

<sup>44</sup> Mathe C. P. Suppurative Orchitis. Its Diagnosis and Treatment. *J. Urol.* 34:324 (Oct.) 1935.

TABLE 1.—Analysis of Preoperative Control Experiments on Gastric Motility\*

Date of Experiment	Duration of Experiment	Number of Periods of Quiescence		Duration of Periods of Activity	Contractions					Comment
		1	2		Type	Number	Duration	Interval Between	Amplitude	
9/13/34	5 hr 30 m	1		61 m	Low grade II	Instestimable 205	Instestimable Max 1 m Min 5 s	5 s Max 45 s Min 2 s	Low grade Max 3.5 cm Min 1.2 cm	Fluctuations in gastric tonus Following this period of activity, the stomach went into a state of quiescence lasting 61 minutes
10/ 7/34	4 hr 30 m	1		10 m 20 s 30 m 55 s 20 m	Low grade II	Instestimable 86	Instestimable Max 45 s Min 18 s Max 27 s Min 18 s	Instestimable Max 1 m 35 s Min 27 s Max 2 m 50 s Min 27 s	Low grade Max 5.5 cm Min 0.7 cm Max 9 cm Min 2 cm	Tonus changes resembling Traube Herring waves
10/10/34	5 hr	1		29 m 10 s 29 m 55 s 39 m 25 s 23 m 50 s	I II I I	Instestimable 49	18 s (av) Max 40 s Min 18 s Instestimable	Max 27 s Min 5 s Max 1 m 35 s Min 20 s Instestimable	Low grade Max 7.5 cm Min 1.5 cm Low grade	
11/ 4/34	3 hr 45 m	1		20 m 30 s	I	Instestimable	Instestimable	Instestimable	Low grade	Tonus changes resembling Traube Herring waves
		1		82 m 35 s 57 m 55 s	I II	Instestimable 76	Instestimable Max 54 s Min 18 s	Instestimable 44 s (av)	Low grade Max 15.5 cm Min 2 cm	Fluctuations in gastric tonus
11/ 6/34	3 hr 30 m	1		30 m 55 s 27 m 5 s	I II	Instestimable 35	Instestimable Max 18 s Min 5 s	Instestimable 5 s (av)	Low grade Max 15 cm Min 1 cm	
		1		39 m	I and II	Instestimable	Instestimable	Instestimable	Max 3.5 cm Min 0.8 cm	
11/ 7/34	4 hr 5 m	1		89 m 18 m	I I II	Instestimable 35	Instestimable Instestimable 20 (av)	Instestimable Instestimable Max 2 m 30 s Min 40 s	Low grade Low grade Max 2.2 cm Min 1.1 cm	Low grade tonus changes Low grade tonus changes

instances hernias persisted three months after descent of the testes. Through these hernias the testes could be pushed back into the inguinal canal. In each instance the testes tended to increase in size after their descent into the scrotum, and in 3 cases the affected organ could not be differentiated from the normal one on physical examination three months after cessation of treatment. The others remained smaller than normal. All of them increased in degree of firmness. Assays of the urine of the 5 boys who were above the age of 11 years for testes hormone showed no definite change after treatment. This was expected since all of the patients except 1 had normal secondary sexual characteristics, and in this instance the departure from normal was not extreme.

The dosage of the extract of the urine of pregnant women was more than that used in most of the other cases previously reported. No reactions were encountered except slight erythema at the site of the injection. With this system of dosage, descent of the testis usually occurred during the third week of treatment. The period during which the hormone is administered as well as the total number of units given is a factor. Although these cases were unselected, it is probable that there was an element of chance in determining the high percentage of cases in which descent occurred, since it is likely that in a certain group of cases the testes are prevented from descending by mechanical block such as that caused by the adhesions commonly found at operation. No conclusions could be made in regard to the mechanism that was responsible for the descent of the testes.

#### PENIS

*Preputial Stone*—Ingraham<sup>47</sup> stated that preputial stone occurs in those cases of phimosis, usually congenital, in which the orifice for the passage of urine becomes so small that stagnation occurs in the preputial sac, which is distended by pressure of urine from the bladder. The anterior portion of the urethra becomes dilated, and the bladder hypertrophies and enlarges. Hydro-ureter may develop if the condition continues over a long period. In the presence of infection, the debris from which forms a nucleus, stagnation of urine is likely to result in the deposit of urinary salts to form calculi in the kidneys, bladder or preputial sac. The calculi formed high in the urinary tract are caught by the phimosed prepuce if they are carried downward by the flow of urine, and the result is the same as though they were formed in the latter situation. The stones consist of organic matter impregnated with calcium or magnesium phosphate or urate, occasionally of ammonium salt or uric acid. They increase more or less rapidly in size as successive

<sup>47</sup> Ingraham, N. R., Jr. Preputial Calculus, a Clinical Rarity. Report of a Case, I. A. M. A 105:106 (July 13) 1935.

TABLE 2—Analysis of Experiments on Gastric Motility After Resection of the Left Splanchnic Nerves

Date of Experiment	Duration of Experiment	Number of Periods of Quiescence	Duration of Periods of Quiescence	Number of Periods of Activity	Duration of Periods of Activity	Contractions				Comment
						Type	Number	Duration	Interval Between	
12/ 6/31	5 hr 15 m	1	9 m	1	15 m 5 s	II	13	Max 1 m 10 s Min 40 s	Max 1 m 30 s Min 30 s	Max 3.2 cm Min 0.7 cm
		1	14 m 10 s	1	23 m 20 s	II	21	Max 50 s Min 5 s	Max 1 m Min 5 s	Max 3.5 cm Min 1 cm
		1	21 m 15 s	1	30 m 45 s	II	22	Max 55 s Min 20 s	Max 1 m 25 s Min 10 s	Max 4.1 cm Min 1.1 cm
		1	21 m 30 s	1	28 m 30 s	II	18	Max 40 s Min 5 s	Max 2 m 35 s Min 5 s	Max 3.8 cm Min 1.1 cm
		1	22 m 10 s	1	31 m 25 s	II	19	Max 50 s Min 30 s	Max 3 m Min 15 s	Max 3.5 cm Min 0.8 cm
		1	03 m 45 s							
12/ 7/34	4 hr 45 m	1	10 m 20 s	1	66 m 30 s	I	Inestimable	Inestimable	Inestimable	Max 2.3 cm Min 0.5 cm
		1	0 m 25 s	1	43 m 25 s	I and II	18	Max 35 s Min 5 s	Max 3 m 25 s Min 1 m 10 s	Max 4 cm Min 1.2 cm
		1	57 m 50 s	1	75 m 55 s	I and II	16	Max 45 s Min 15 s	Max 1 m 25 s Min 55 s	Max 3.7 cm Min 1.5 cm
		1	17 m 10 s	1	75 m 10 s	I and II	Inestimable	Max 50 s Min 20 s	Max 3 m Min 20 s	Max 7.3 cm Min 1 cm
12/ 9/34	4 hr	1	97 m 45 s	1	35 m 25 s	1	Inestimable	Inestimable	Inestimable	Low grade
		1	34 m	1	73 m	I and II	45	Max 1 m Min 20 s	Max 1 m 25 s Min 10 s	Max 4.5 cm Min 1.4 cm
12/10/34	6 hr 10 m	1	19 m 10 s	1	14 m 45 s	II	6	Max 55 s Min 30 s	Max 2 m Min 1 m	Max 1.1 cm Min 0.7 cm
		1	43 m 25 s	1	55 m	I and II	32	Max 1 m Min 45 s	Max 2 m Min 1 m 20 s	Max 2.5 cm Min 0.5 cm
		1	11 m 55 s	1	52 m	I and II	24	Max 50 s Min 20 s	Max 1 m 30 s Min 35 s	Max 4.1 cm Min 0.6 cm

During each period of quiescence there was evidence of changes of tonus

Experiment terminated

Almost continuous gastric activity with a few severe contractions

16 m after onset of experiment, 40 units of insulin was administered without any appreciable change in motility

## EFFECT OF BILATERAL RESECTION OF THE SPLANCHNIC NERVES ON GASTRIC MOTILITY IN MAN

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During the past fifteen years numerous attempts have been made to correct certain abnormal physiologic states by the surgical interruption of various nervous pathways. Among these operative procedures, unilateral and bilateral resections of the splanchnic nerves have been frequently employed. In 1921 Jean<sup>1</sup> performed resection of the splanchnic nerves for the relief of pyloric spasm, hyperacidity and gastric hypersecretion. Danielopolu<sup>2</sup> recommended the same procedure for the management of hypertension. For a few years resection of the left splanchnic nerves was considered adequate for the production of clinical relief in arterial hypertension. Craig and Brown<sup>3</sup> performed unilateral and bilateral resection of the major and minor splanchnic nerves for the relief of essential hypertension in young persons and concluded that it was a justifiable procedure in the early stages of the severe progressive form. The interruption of other nervous pathways<sup>4</sup> has been attempted

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1 Jean, G. Les nerfs splanchniques au point de vue chirurgical, *Arch de med et pharm* 111 292, 1921.

2 Danielopolu, quoted by Craig and Brown<sup>3</sup>.

3 Craig, Winchell, and Brown, George E. Unilateral and Bilateral Resection of the Splanchnic Nerves. Its Effects in Cases of Essential Hypertension. *Ann Surg* 54 577 (Oct) 1934.

4 Page, C. I., and Heuer, George J. A Surgical Treatment of Essential Hypertension. I. Clin Investigation 14 22 (Jan) 1935, The Effect of Renal Denervation on the Level of Arterial Blood Pressure and Renal Function in Essential Hypertension, *ibid* 14 27 (Jan) 1935.



TABLE 2—Analysis of Experiments on Gastric Motility After Resection of the Left Splanchic Nerves—Continued

Date of Experiment	Duration of Experiment	Number of Periods of Quiescence	Duration of Periods of Activity	Number of Periods of Activity	Constrictions			Amplitude	Comment
					Type	Number	Interval Between		
2/ 5/35	5 hr			1	II and III	Instimable	Instimable	Max 3.5 cm Min 0.5 cm	Constant, moderately severe motility no periods of quiescence, gastric tetany and type III
2/ 8/35	4 hr	1	9 m	1	I and III	Instimable	Instimable	Max 2.5 cm Min 0.5 cm	Period terminated in gastric tetany
2/11/35	5 hr 7 m	1	12 m 40 s	1	II	200	Max 1 m 10 s Min 10 s	Max 1.5 cm Min 1 cm	Constant severe motility with periods of gastric tetany
2/13/35	5 hr	1	9 m	1	III	Instimable	Instimable	Max 1 cm Min 1.5 cm	Experiment terminated during period of activity
2/15/35	5 hr 22 m	1	11 m 30 s	1	II	169	Max 1 m 45 s Min 10 s	Max 3.5 cm Min 1 cm	Period of activity followed by quiescence during which an occasional contraction was observed
2/19/35	6 hr 5 m	1	15 m 45 s	1	II and III	Instimable	Instimable	Max 1.5 cm	Periods of incomplete tetany observed this followed by period of type II contractions lasting 20 m 25 s
2/20/35	5 hr 5 m	1	48 m 15 s	1	III	Instimable	Max 1 m 15 s Min 15 s	Max 5 cm Min 1.5 cm	Period of tetany lasting 36 m 15 s, one period of tetany lasting 5 m 20 s
2/27/35	6 hr 45 m	1	10 m 45 s	1	III	Instimable	90 s	2.5 cm	Contractions were uniform stomach showed continuous motility
		1	48 m 40 s	1	II and III	Instimable	Max 1 m 25 s Min 15 s	Max 3 cm Min 1.5 cm Min 5 cm Min 2 cm	Periods of tetany lasting 10 m
		1	344 m	1	II and III	Instimable	Max 1 m 15 s		Duration of type III contraction 2 hr 9 m
						285			Duration of type II contraction 1 hr 15 m

## PROCEDURE

The patient, a cooperative white man of 28, was trained to swallow a condom balloon attached to the end of a Rehfuß tube in place of the metal bulb. The tube was then connected to a bromoform manometer. In order that we might know accurately the location of the balloon in the stomach, a balloon coated with barium sulfate<sup>9</sup> was first swallowed, and its position was ascertained by means of the fluoroscope and by roentgenograms (fig 1). The length of rubber tubing from this position to the incisor teeth was 54 cm. This distance was kept constant throughout



Fig 1—Roentgenogram demonstrating the balloon coated with barium sulfate in the stomach

the observations. At the beginning of each experiment, the balloon was inflated to a pressure of 2 cc of bromoform, and gastric motility was recorded on a slowly revolving kymograph (fig 2). An automatic timer, recording every five seconds, was incorporated into the system. This made it possible to determine accurately the duration of and the interval between contractions. Observations were made in the morning, fourteen hours after the preceding meal, and were continued for a period of about five hours.

<sup>9</sup> Carlson, A. J. *The Control of Hunger in Health and Disease*, Chicago, University of Chicago Press, 1916.

TABLE 3—Analysis of Experiments on Gastric Motility After Resection of the Right Splanchnic Nerves

Date of Experiment	Duration of Experiment	Number of Periods of Activity			Type	Contractions			Comment
		Quiescence	Periods of Quiescence	Duration of Activity		Number	Duration	Interval Between	Amplitude
3/11/35	5 hr	1	1	16 m 30 s	II and III	201	Instimable Max 1 m Min 30 s	Instimable Max 3 m 20 s Min 40 s	Instimable Max 8.5 cm Min 2 cm
3/13/35	5 hr 35 m	1	1	27 m 266 m	I and II	173	Instimable Max 1 m Min 20 s	Instimable Max 2 m 10 s Min 1 m	Low grade Max 5 cm Min 2 cm
3/15/35	5 hr 30 m	1	1	27 m	II	26	Max 1 m Min 20 s	Max 1 m Min 15 s	Max 3.5 cm Min 2 cm
		1	1	207 m	II	176	Max 50 s Min 20 s	Max 2 m Min 30 s	Max 5.5 cm Min 1.2 cm
3/19/35	5 hr	1	1	300 m	II	239	Max 2 m Min 25 s	Max 3 m 10 s Min 30 s	Max 5.5 cm Min 2 cm
3/22/35	5 hr 15 m	1	1	5 m	II	29	Max 25 s Min 15 s	Max 1 m Min 10 s	Max 6 cm Min 3.5 cm
		1	1	25 m	II	65	Max 1 m 5 s Min 10 s	Max 1 m 10 s Min 5 s	Max 9.5 cm Min 3 cm
		1	1	104 m 25 s	II	16	Max 1 m 15 s Min 20 s	Max 6 m 20 s Min 20 s	Max 11 cm Min 1.5 cm
		1	1	19 m 15 s	II	22	Max 55 s Min 30 s	Max 1 m 5 s Min 30 s	Max 7.5 cm Min 2.5 cm
		1	1	23 m 45 s	II	75	Max 45 s Min 25 s	Max 1 m Min 20 s	Max 7 cm Min 4 cm
		1	1	80 m 55 s	II		Max 2 m Min 20 s	Max 1 m 55 s Min 30 s	Max 6.5 cm Min 3 cm
3/24/35	1 hr 30 m	Continuous relatively low grade motility			type I and type II contractions				
3/27/35	5 hr	1	1	300 m	I and II	Instimable	Max 1 m Min 10 s	Max 50 s Min 10 s	Max 3 cm Min 2 cm

Contractions occurred rapidly

Terminated in activity

No quiescent periods

Short periods of severe motility interrupted by short periods of quiescence

Type I and II could not be clearly differentiated

11/ 4/24	1 hr 10 m	1	40 m	1	63 m	I	82	Max 30 s Min 20 s Instimable Max 30 s Min 20 s	Max 1 m 10 s Min 15 s Instimable Max 1 m 20 s Min 5 s	Max 11 cm Min 16 cm Low grade Max 11 cm Min 1 cm	Low grade tonus changes This was followed by a period of quiescence during which time the experiment was dis- continued
11/ 9/24	2 hr 45 m	1	33 m 10 s	1	107 m	I and II	Instimable 140	Instimable	Instimable	Low grade	
11/10/24	3 hr 10 m	1	0 m 10 s	1	37 m 40 s 97 m 20 s	I II	Instimable 93	Instimable 18 s (av)	Instimable Max 6 m Min 9 s Instimable	Low grade Max 13 1 cm Min 15 cm Low grade	
11/12/ 4	5 hr 5 m	1	13 m	1	65 m 184 m	I I and II	Instimable Remarks	Instimable Max 50 s Min 20 s	Instimable Max 40 s Min 20 s	Low grade Max 17 cm Min 05 cm	One violent contraction 8 m before end of experiment amplitude 87 cm otherwise low grade activity
11/17/24	1 hr 50 m	1	36 m 4 s 17 m 25 s	1	61 m	I II II	Instimable 99 37	Instimable Max 1 m 10 s Min 20 s Max 20 s Min 10 s	Instimable Max 3 m 20 s Min 3 m Min 30 s	Low grade Max 11 cm Min 1 cm Max 86 cm Min 07 cm	Because of the variability of the type of contractions the number was not counted The period of quiescence merged with the period of low grade activity these periods could not be demarcated
11/18/24	5 hr										Experiment terminated at this time
11/21/24	2 hr 5 m										
11/22/ 4	3 hr 10 m	1	6 m 1 s 60 m 4 s 165 m	1 1	60 m 4 s 165 m	I I and II	Instimable Remarks	Instimable Max 1 m Min 10 s	Instimable Max 2 m Min 10 s	Low grade Max 5 cm Min 07 cm	The number of contractions could not be counted, many contractions merged with deep respirations which obscured the actual gastric contraction

\* In this table and in tables 2 and 3, m indicates minutes, s, seconds, Min minimum, and Max, maximum

TABLE 3—Analysis of Experiments on Gastric Motility After Resection of the Right Splanchnic Nerves—Continued

Date of Experiment	Duration of Experiment	Number of Periods of Quiescence		Duration of Quiescence	Number of Periods of Activity		Duration of Activity	Contractions				Comment	
		1	2		1	2		I type	Number	Duration	Interval Between		Amplitude
4/19/35	4 hr 45 m	1		22 m	1	256 m		II	202	Max 1 m Min 35 s	Max 1 m 35 s Min 5 s	Max 6 cm Min 3 cm	
4/21/35	5 hr 40 m				1	94 m		II	92	Max 50 s Min 20 s	Max 40 s Min 20 s	Max 9 cm Min 2 cm	
		1		47 m	1	199 m		II	103	Max 1 m Min 10 s	Max 3 m Min 5 s	Max 10 cm Min 3 cm	Intense motility throughout observation period
4/23/35	5 hr	1		12 m	1	67 m		II and III	Instimable	Instimable	Instimable	Max 4 cm Min 2 cm Max 4 cm Min 1.5 cm	This period ended in gastric tetany
4/24/35	5 hr 20 m				1	111 m		II	109	Max 40 s Min 10 s	Max 1 m 35 s Min 10 s	Max 12.5 cm Min 2 cm	Intense motility
		1			1	59 m		I	Instimable	Instimable	Instimable	Max 6.5 cm Min 2 cm	
		1			1	48 m		II	63	Max 1 m 10 s Min 15 s	Max 1 m 30 s Min 20 s	Max 6.5 cm Min 2 cm	
					1	102 m		I and II	Instimable	Instimable	Instimable	Max 3.5 cm Min 1.5 cm	Continuous motility throughout observation period
4/26/35	5 hr	1		9 m	1	79 m		I II and III	Instimable	Instimable	Instimable	Max 3.5 cm Min 1 cm	Period ended in gastric tetany, terminal period of type II motility
		1			1	212 m		I and II	97	Max 50 s Min 40 s	Max 1 m 20 s Min 10 s	Max 4.5 cm Min 2 cm	
4/28/35	5 hr 20 m				1	320 m		II	337	Max 50 s Min 5 s	Max 1 m Min 10 s	Max 4 cm Min 2 cm	Continuous type II motility throughout observation period
4/29/35	5 hr	1		32 m	1	69 m		I, II and III	Instimable	Instimable	Instimable	Max 5 cm Min 1.5 cm Max 6 cm Min 3 cm	Period ended in gastric tetany
		1			1	229 m		II	198	Max 1 m Min 30 s	Max 1 m 40 s Min 25 s	Max 5 cm Min 1.5 cm Max 6 cm Min 3 cm	

12/12/34	5 hr	1	31 m 25 s	1	22 m 20 s	II	22	Max 55 s Min 5 s Max 50 s Min 15 s	Max 25 s Min 0 s Max 2 m Min 25 s	Max 43 cm Min 1 cm Max 54 cm Min 11 cm	
12/13/34	5 hr	1	30 m 10 s	1	110 m 10 s	I and II	41	Max 1 m Min 25 s Max 1 m Min 5 s Max 1 m Min 25 s	Max 6 m 20 s Min 1 m Max 4 m Min 1 m 30 s Max 4 m 20 s Min 1 m 25 s	Max 39 cm Min 0.6 cm Max 12 cm Min 2 cm Max 18 cm Min 13 cm	Experiment terminated
12/11/34	5 hr 5 m	1	107 m	1	190 m	II	92	Max 1 m 15 s Min 15 s	Max 5 m Min 1 m	Max 18 cm Min 1 cm	
1/1/35	3 hr 25 m	1	11 m 10 s	1	175 m 35 s	II	143	Max 50 s Min 20 s Inestimable	Max 1 m 35 s Min 20 s Inestimable	Max 47 cm Min 0.8 cm Low grade	82 m after start of experiment patient was given injection of atropine, 1/150 grain, no alteration in gastric motility
1/5/35	4 hr	1	11 m 10 s	1	210 m	II	228	Max 1 m Min 10 s	Max 2 m 20 s Min 30 s	Max 15 cm Min 0.6 cm	5 m after onset of experiment blood sugar drawn, period of quiescence followed
1/10/35	4 hr 3 m	1	22 m 10 s	1	172 m	I and II	170	Max 1 m 10 s Min 20 s	Max 2 m Min 5 s	Max 9 cm Min 1 cm	Experiment terminated at this time
1/24/35	4 hr 4 m	1	10 m 25 s	1	227 m	II and III	91	Max 1 m 35 s Min 15 s	Max 2 m 25 s Min 10 s	Max 5 cm Min 14 cm	Severe motility lasting 105 m 35 s, type III contractions observed, type II contraction for 120 m, 10 s experiment ended during period of quiescence
1/26/35	5 hr	1	21 m	1	07 m	III	Inestimable	Inestimable	Inestimable	Max 7.5 cm Min 1.5 cm 1 cm	Severe motility, period terminated in gastric tetany
1/26/35	5 hr	1	21 m	1	215 m	II and III	168	Max 10 s Min 10 s	Max 2 m 15 s Min 15 s	Severe motility at beginning of period, last 1m, 60 m, type II contractions for 155 m	
1/30/35	5 hr	1	8 m 15 s	1	44 m	III	Inestimable	Inestimable	Inestimable	Max 3 cm Min 0.5 cm	Severe motility ending in gastric tetany
1/30/35	5 hr	1	15 m 40 s	1	7 m 10 s	III	Inestimable	Inestimable	Inestimable	Max 4 cm Min 0.5 cm Max 6 cm Min 1.5 cm	Severe motility ending in gastric tetany

certain instances quiescence, appearing between periods of activity, exhibited an abrupt onset and an abrupt cessation "Gastric respirations" frequently were associated with low grade fluctuations in tonus (fig 4), followed by feeble contractions which became increasingly severe, making it difficult to differentiate between the cessation of quiescence and the onset of activity

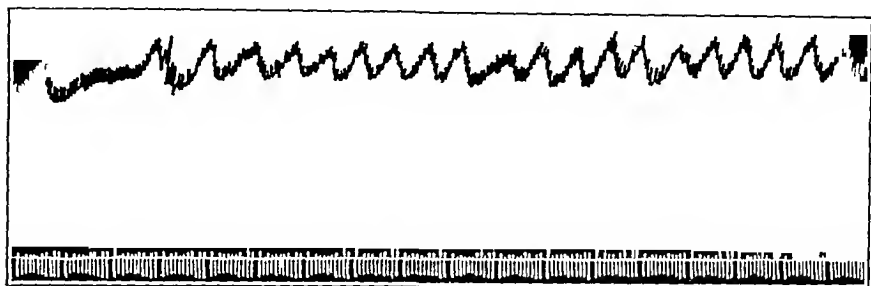


Fig 4—Tracing made on Nov 16, 1934, showing feeble changes of tonus

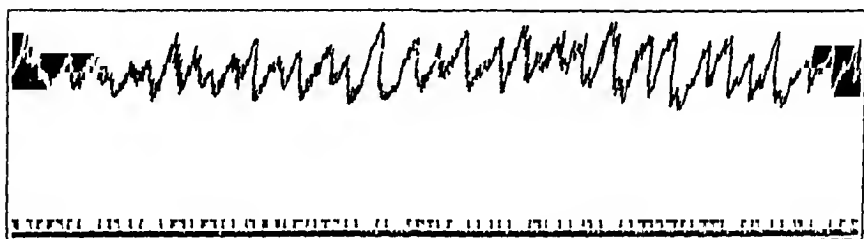


Fig 5—Type I contractions

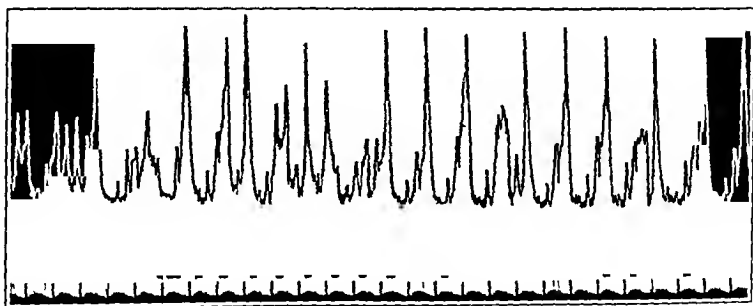


Fig 6—Type II contractions

Gastric motility was analyzed according to Carlson's criteria.<sup>9</sup> Three types of contraction were recognized, depending on the degree of gastric tonus. Type I denotes a state of low grade tonus (fig 5). Actual contractions are feeble, and the amplitude is low. This type of motility was commonly observed during the control period.

Type II contractions are associated with a relatively strong gastric tonus. These contractions occur in rapid succession without any marked intervening pause (fig 6). Contractions of this type were observed

Fifteen preoperative control observations were made (table 1) prior to bilateral resection of the splanchnic nerves. This was done in two stages. On Nov. 28, 1934 resection of the left splanchnic nerves was accomplished. Studies of gastric motility were resumed eight days after the operation. Twenty-one postoperative observations (table 2) were made under the same conditions as obtained during the control period. Resection of the right splanchnic nerves was then performed on March 4, 1935 the same technique being utilized as in the previous operation. Studies of gastric motility were again undertaken about a week postoperatively, and twenty-five subsequent observations (table 3) were made.

*Stage I Resection of the Left Splanchnic Nerves, Nov. 28, 1934*—With the patient under gas anesthesia, a curved paravertebral incision was made over the inner ends of the ninth, tenth and eleventh ribs. The longitudinal muscles were carefully separated from their costal attachments and were retracted laterally. The inner ends of the ninth, tenth and eleventh ribs were freed, disarticulated and resected. To increase the exposure points of the transverse processes were

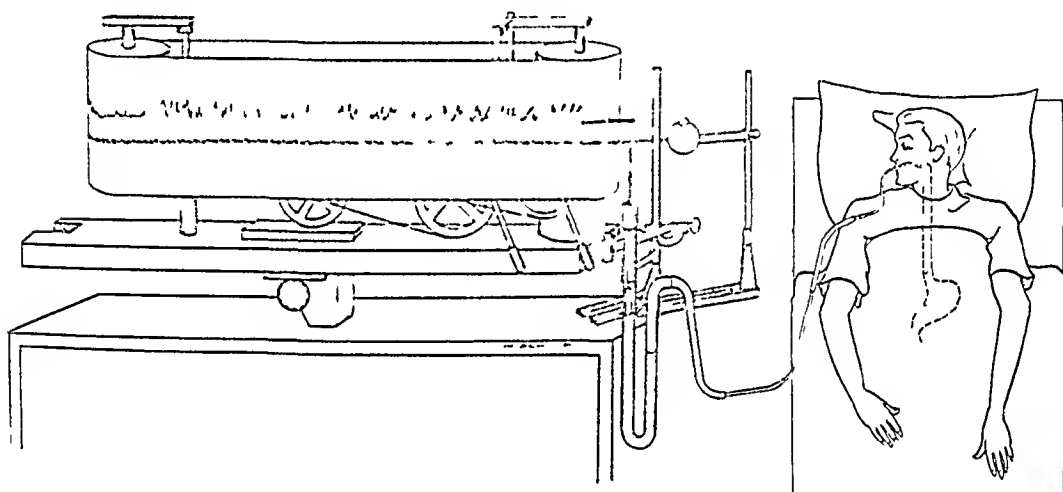


Fig. 2—Diagram of apparatus used to record gastric motility

removed with a rongeur. The thin pleura was retracted laterad. The posterior mediastinum was then entered. The splanchnic nerves were identified. A number of branches extending through the diaphragm were found. These arose from the ganglionated cord. In all there were two large and five small branches. These were dissected, and 3 to 5 cm. segments were resected. All connections with the ganglionated cord were severed. The region was thoroughly explored for accessory splanchnic nerves. None were found. The wound was closed in layers. Throughout the operation no complication was encountered. Immediately after the resection of the left splanchnic nerves there was no precipitous drop in the blood pressure. The postoperative convalescence was uncomplicated. Shortly after the operation the blood pressure gradually fell to a low level, but at no time were untoward symptoms apparent.

*Stage II Resection of the Right Splanchnic Nerves, March 4, 1935*—The technique and details of this stage were essentially the same as those in the first stage. No complications occurred, and recovery was rapid. Postoperatively, the drop in blood pressure was not so marked as that which occurred after the first



between contractions. The number of contractions during a period of observation was increased. The reason for this was the prolonged duration of activity. There was a slight but definite increase in the amplitude of contractions. Type III contractions were common. The rapidity

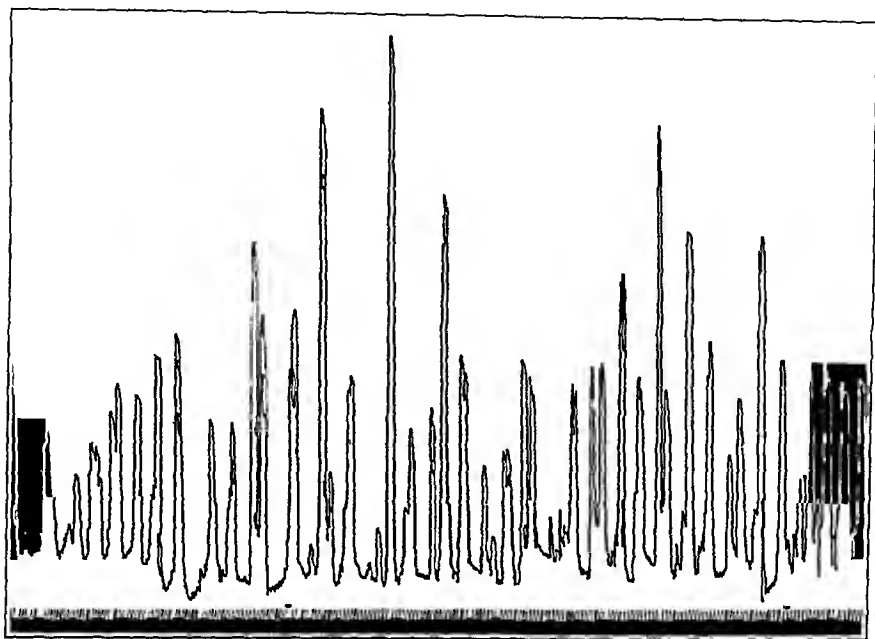


Fig 8—Tracing made on Feb 13, 1935, showing intense gastric motility after resection of the left splanchnic nerves. The maximal amplitude of contractions was 14 cm.

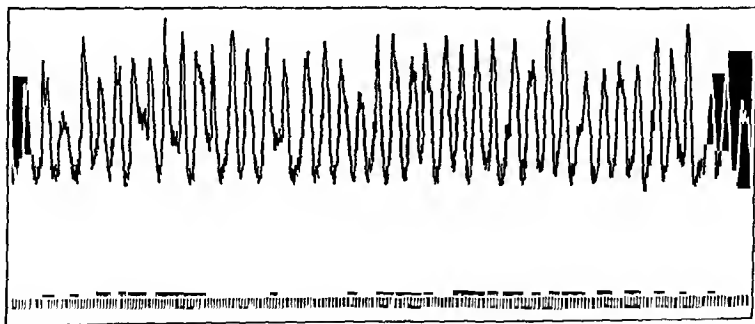


Fig 9—Tracing made on Feb 27, 1935, showing persistent gastric motility after resection of the left splanchnic nerves. The duration of the period of activity was three hundred and forty-four minutes.

with which these contractions appeared made it impossible to evaluate accurately the number of, the duration of, and the interval between, contractions. Occasionally there was a blending of type II and type III, making it difficult to differentiate between the two.

3/29/35	5 hr	1	300 m	I and II	Instimable	Max 2 m Min 25 s	Max 1 m Min 20 s	Max 4 cm Min 2 cm	
3/31/35	1 hr 15 m	1	47 m	II and III	Instimable	Instimable	Instimable	Period ended in gastric tetany	
	1	1	188 m	I and II	Instimable	Max 1 m 40 s Min 30 s	Max 3 m Min 20 s	Max 4 cm Min 2 cm	
4/1/35	5 hr	1	23 m	II and III	Instimable	Instimable	Instimable	Period ended in gastric tetany	
	1	1	263 m	II	273	Max 1 m Min 30 s	Max 1 m 10 s Min 35 s	Max 5.5 cm Min 1.5 cm	
4/2/35	5 hr	1	61 m	II and III	52	Max 15 s Min 10 s	Max 3 m Min 20 s	Max 9 cm Min 2 cm	
	1	1	106 m	II	67	Max 30 s Min 15 s	Max 2 m 15 s Min 40 s	Max 9 cm Min 2 cm	
	1	1	52 m	II	33	Max 50 s Min 15 s	Max 3 m Min 15 s	Max 6 cm Min 2 cm	Terminated in activity
4/3/35	5 hr	1	88 m	II and III	Instimable	Max 55 s Min 10 s	Max 55 s Min 20 s	Max 5.5 cm Min 1.5 cm	
	1	1	143 m	I and II	112	Max 1 m Min 20 s	Max 1 m 20 s Min 25 s	Max 4.5 cm Min 1.5 cm	
4/4/35	5 hr	1	300 m	I and II	272	Max 1 m 10 s Min 20 s	Max 30 s Min 20 s	Max 5 cm Min 2 cm	Type I 106 m Type II 194 m
4/5/35	5 hr 20 m	Continuous motility type I and II contractions							
4/6/35	5 hr 10 m	1	46 m	II	47	Max 50 s Min 25 s	Max 40 s Min 20 s	Max 4.5 cm Min 2 cm	Period terminated in gastric tetany
	1	1	185 m	I	170	Max 1 m 10 s Min 20 s	Max 1 m 40 s Min 40 s	Max 4.5 cm Min 2 cm	
4/15/35	5 hr 15 m	1	58 m	I, II, III and III	Instimable	Instimable	Instimable	Period ended in gastric tetany	
	1	1	202 m	I and II	276	Max 1 m 15 s Min 5 s	Max 1 m Min 5 s	Max 1.5 cm Min 12 cm	
4/16/35	5 hr	1	160 m	I and II	Instimable	Instimable	Instimable	Max 3 cm Min 1.5 cm	
	1	1	140 m	II	280	Max 50 s Min 20 s	Max 30 s Min 10 s	Max 4 cm Min 2.5 cm	
4/18/35	3 hr 30 m	1	210 m	II	212	Max 40 s Min 5 s	Max 30 s Min 5 s	Max 4.5 cm Min 2 cm	

described. In some experiments there was complete abolition of relative quiescence, the entire period of observation being one of intense gastric motility. Many experiments were similar to those following the resection of the left splanchnic nerves in that there was an initial short period of activity terminating in tetany. This was followed by a very short period of quiescence, after which the motility was continuous throughout the period of observation. No change of any magnitude was observed in the type of, the duration of, the interval between, or the amplitude of, contractions when they were compared with the results following resection of the left splanchnic nerves.

#### COMMENT

Abdominal and extra-abdominal surgery are frequently complicated by morbid physiologic processes which if uncorrected may proceed to a fatal termination.<sup>11</sup> Acute dilatation of the stomach and paralytic ileus still present pressing problems in their etiology and management.<sup>12</sup> The investigations of Brunemeier and Carlson<sup>13</sup> and Dragstedt<sup>12</sup> indicate that surgical intervention on the gastro-intestinal tract is associated with interference with efferent and afferent nervous pathways. These play an important rôle in the development of complications.

The work reported in this paper was undertaken to establish certain basic facts, on which can be constructed further investigation. This may yield information regarding the rôle of the mechanism of the gastro-intestinal motor nerves in the production and management of these perverted physiologic conditions.

The effects of bilateral resection of the splanchnic nerves on the gastric motility of dogs indicated an increase in gastric tonus and an augmentation of the contractions. Motility frequently was continuous throughout a period of observation of from two to four hours.<sup>9</sup> The results of our experiments on our patient confirm these findings. Tables 1, 2 and 3 illustrate that after bilateral resection of the splanchnic nerves there is a definite augmentation of gastric activity. Occasionally the motility after resection of the splanchnic nerves did not differ from that observed during the control period.

The vagus is considered the primary motor nerve to the stomach. Therefore, it would seem that the augmentation in gastric tonus sub-

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11 Dragstedt, Lester R. Failure of Reabsorption of Gastric and Pancreatic Juice as a Pathogenic Factor in Some Gastro-Intestinal Disturbances, *Am J Surg* **11** 544, 1931.

12 Dragstedt, Lester R., Montgomery, Laurence, Ellis, James C., and Matthews, Warren B. The Pathogenesis of Acute Dilatation of the Stomach, *Surg, Gynec & Obst* **52** 1075, 1931.

13 Brunemeier, E. H., and Carlson, A. J. Reflexes from the Intestinal Mucosa to the Stomach, *Am J Physiol* **36** 191, 1914.

stage. There has been a gradual decrease in the patient's requirement of insulin. At present the condition is controlled with 30 units daily, in contrast to 100 units, which he required prior to surgical intervention.

### RESULTS

The effects of bilateral resection of the splanchnic nerves on gastric motility were evaluated according to the following criteria: (1) duration of the experiment, (2) number of periods of quiescence, (3) duration of quiescence, (4) number of periods of activity, (5) duration of activity, (6) number of contractions during a period of activity, (7) duration of the contractions, (8) interval between contractions, (9) amplitude of contractions and (10) type of contractions.

The data accumulated during the control period are presented in table 1.



Fig 3—Kymographic tracing made on Oct 7, 1934, showing relative gastric quiescence at the beginning of a period of observation. Respiratory movements or "gastric respirations" can be noted.

The normal empty living stomach is rarely, if ever, in a state of absolute quiescence. Experimentation<sup>9</sup> reveals rhythmic periods of motility alternating with periods of relative quiescence. During these there may be an absence of actual contractility, but a certain degree of gastric tonus is always present. Kymographic records, obtained by the balloon method during periods of relative quiescence, frequently reveal the influence of diaphragmatic excursions. These have been termed "gastric respirations" (fig 3). With the bromoform manometer it is possible to record even the pulsations of the intra-abdominal vessels, superimposed on the fluctuations in gastric tonus.

In our experiments, periods of relative quiescence often occurred at the beginning. This may have been due to reflex motor inhibition of the stomach, subsequent to esophageal and gastric stimulation.<sup>10</sup> In

10 Carlson, A. J. Gastric Hunger Contractions Inhibited Reflexly from the Mouth, *Am J Physiol* **31** 212, 1913, Influence of Stimulation of the Gastric Mucosa on Gastric Hunger Contractions, *ibid* **32** 245 and 389, 1913.

The gastric motor mechanism is frequently augmented in severe uncontrolled diabetes. This observation was made by Luckhardt<sup>18</sup> on untreated diabetic dogs and on man. In the preinsulin days Allen<sup>19</sup> observed that the polyphagia of diabetes in man often disappeared simultaneously with the disappearance of acidosis and glycosuria. These clinical and laboratory data indicate that there exists a relationship between gastric motility and the blood sugar level.

Bulatao and Carlson<sup>20</sup> found that the gastric hypermotility of diabetic dogs often disappeared when the blood sugar level was restored to normal by insulin therapy. These authors suggested the possibility that under ordinary conditions gastric tonus and the contractions of the empty stomach increase parallel with the reduction of glycogen in the tissues.

The blood sugar level of our patient was well controlled by careful therapy with insulin and dextrose. Occasionally hypoglycemia was observed, but the condition was rectified as soon as it became apparent. Stability of the blood sugar level was of paramount importance in order that the true results of splanchnic resection would not be obscured.

Alvarez<sup>21</sup> reported that after resection of the splanchnic nerves in rabbits the bowel became so sensitive that when it was touched it often contracted to form a firm white cord. Although gastric hypermotility was the predominant feature following bilateral resection of the splanchnic nerves in this patient, clinically there were no untoward manifestations. The postoperative course of this patient, like that of others,<sup>22</sup> was entirely uneventful. There was no evidence of abdominal distress, cramping sensations or colic.<sup>23</sup> Diarrhea was not observed. After each stage there was a lowering of the blood pressure. This was most marked after the first stage. It produced no complications. Although there has ensued a definite reduction of the requirement of insulin, up to the present time insulin cannot be wholly omitted. The effect of bilateral splanchnic resection on the diabetes will be reported in extenso subsequently.

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18 Luckhardt, A. B. The Cause of the Polyphagia of Pancreatic Diabetes, *Am J Physiol* **33** 315, 1914.

19 Allen, F. M. Studies Concerning Diabetes, *J A M A* **63** 939 (Sept 12) 1914, Prolonged Fasting in Diabetes, *Am J M Sc* **150** 480, 1915.

20 Bulatao, E., and Carlson, A. J. The Influence of Experimental Changes in the Blood Sugar Level on Gastric Hunger Contractions, *Am J Physiol* **69** 107, 1924.

21 Alvarez, W. C. Effect of Degenerative Section on the Vagus and Splanchnic Nerves on the Digestive Tract, *Proc Staff Meet, Mayo Clin* **4** 205, 1929.

22 Craig and Brown<sup>3</sup> de Takats and Fenn<sup>6b</sup>

23 Ivy, A. C. The Applied Physiology of Gastro-Intestinal Innervation, *Am J Digest Dis & Nutrition* **1** 845 (Feb) 1935.

frequently. During periods of type II contractions, the number of, the duration of the interval between, and the amplitude of, contractions were determined.

Contractions designated as type III occur when the stomach is in a state of tetany (fig 7). This is characterized by periods of strong and relatively persistent tonus, on which are superimposed a series of rapid contractions. Type III was not observed during the control period. The various types of contractions, as observed, are presented in tables 1, 2 and 3.

The data accumulated subsequent to resection of the left splanchnic nerves are presented in table 2. The first four observations were more or less uniform, in that each exhibited short periods of intense motility

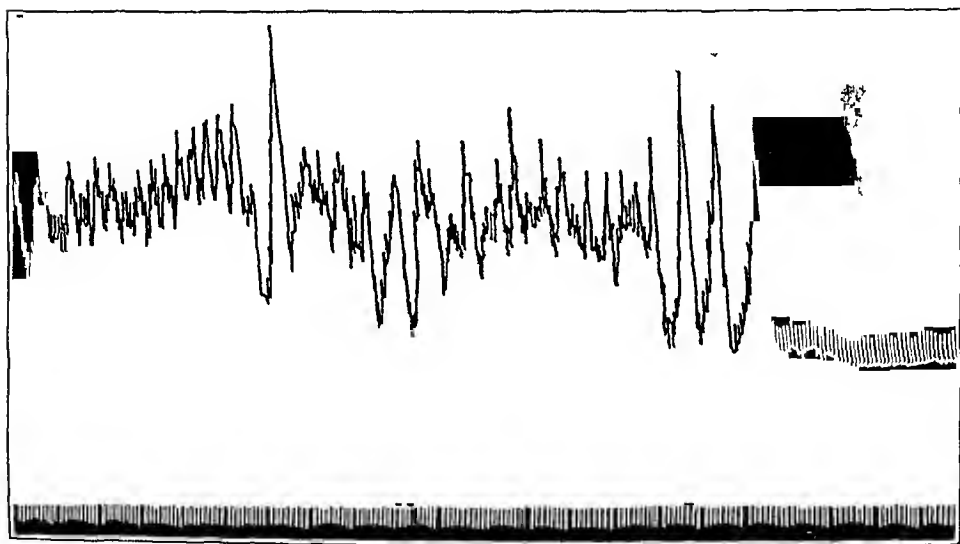


Fig 7—Type III contractions, or gastric tetany

interrupted by short periods of quiescence (fig 8). In the first of these observations the periods of activity were extremely short. The details are tabulated. In the three subsequent observations there was a definite increase in the duration of activity. Finally, in the seventeen subsequent experiments the outstanding feature was the persistent intense gastric motility (fig 9).

Gastric motility was frequently observed at the beginning of the experiment. This persisted for approximately an hour and terminated in a very short period of quiescence the duration of which was approximately ten to twelve minutes. Following quiescence, motility was resumed and usually continued throughout the period of observation. Often the motility ended abruptly in gastric tetany, which lasted approximately ten minutes. In the majority of instances the contractions were of type II, with no great variation in the duration of and the interval

LACTOGENIC SUBSTANCE IN THE HUMAN BREAST  
ITS USE IN EXPERIMENTAL STIMULATION OF MAMMARY SECRETION  
AND ITS ASSAY IN CASES OF CYSTIC DISEASE

CHARLES F GESCHICKTER, M D

AND

DEAN LEWIS, M D

BALTIMORE

That there exists a relationship between the anterior lobe of the hypophysis and lactation has been shown by the work of Gruter and Stricker<sup>1</sup> Investigations which demonstrated the effect of extracts of the anterior lobe of the hypophysis on mammary secretion have been made by Corner,<sup>2</sup> Nelson and Pfiffner,<sup>3</sup> Gardner and Turner<sup>4</sup> and Riddle, Bates and Dykshorn<sup>5</sup> These studies have shown that when the mammary glands of rats, guinea-pigs, rabbits and dogs have been stimulated by the injection of ovarian hormones, injections of extracts of the anterior lobe of the hypophysis may initiate secretory activity

Purified lactogenic substances have been prepared from the anterior lobe of the hypophysis by Turner<sup>6</sup> and his co-workers and by Riddle and his co-workers The use of these extracts and the response of the

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From the Surgical Pathological Laboratory, Department of Surgery, the Johns Hopkins Hospital and University

1 Gruter, F, and Stricker, P Ueber die Wirkung eines Hypophysenvorderlappenhormons auf die Auslösung der Milchsekretion, *Klin Wchnschr* 8 2322, 1929

2 Corner, G W The Hormonal Control of Lactation, *Am J Physiol* 95 43, 1930

3 Nelson, W O, and Pfiffner, J J An Experimental Study of the Factors Concerned in Mammary Gland Growth and Milk Secretion, *Proc Soc Exper Biol & Med* 28 1, 1930

4 Gardner, W U, and Turner, C W The Function, Assay and Preparation of Galactin, a Lactation Stimulating Hormone of the Anterior Pituitary, and an Investigation of the Factors Responsible for the Control of Normal Lactation, *Research Bulletin* 196, Agricultural Experiment Station, University of Missouri, June 1933

5 Riddle, O, Bates, R W, and Dykshorn, S W The Preparation, Identification and Assay of Prolactin—A Hormone of the Anterior Pituitary, *Am J Physiol* 105 191, 1933

6 Turner, C W Personal communication to the authors

The results subsequent to resection of the right splanchnic nerves were similar to those following the first stage (table 3). Twenty-five observations were made. Again the outstanding feature was the persistence of intense gastric motility (fig 10). During some observations

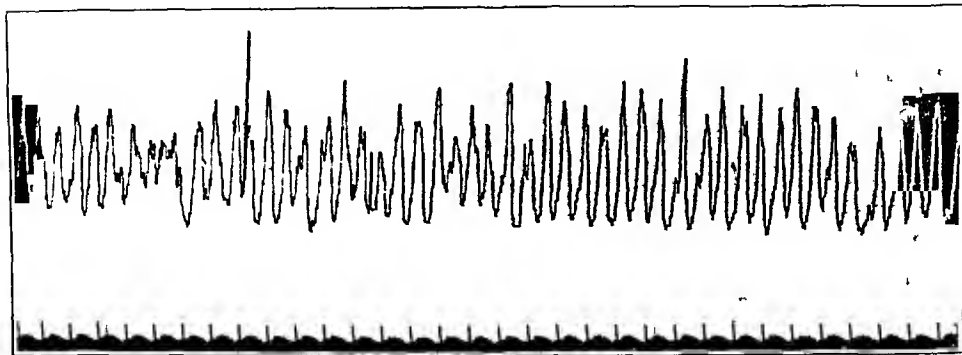


Fig 10—Tracing made on April 16, 1935, showing persistent gastric motility after resection of the right splanchnic nerves. The total duration of activity was three hundred minutes.

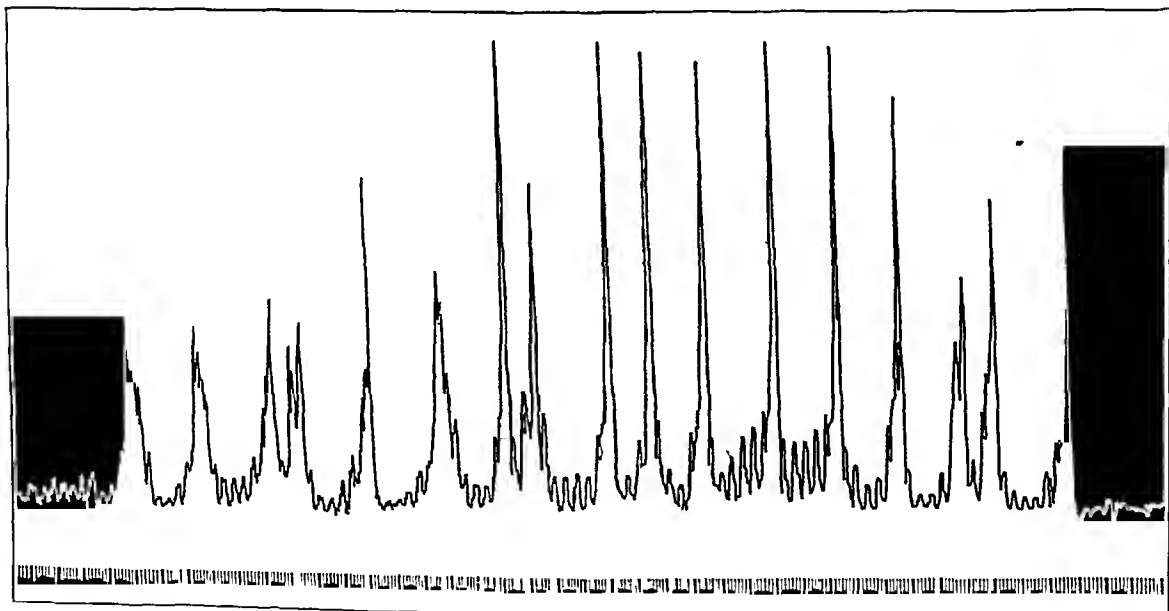


Fig 11—Tracing made on March 22, 1935, showing intense gastric motility after resection of the right splanchnic nerves. The maximal amplitude of contractions was 11 cm.

the contractions were even of sufficient magnitude to rupture the balloon and to force the bromoform almost from the manometer (fig 11). Following them, there was a transitory decrease in gastric tonus, followed by contractions of great amplitude comparable to those just





Fig 1—Photomicrographs of specimens from the breast of a mature female monkey (*A* before and *B* after treatment) which was given injections of 500 rat units of estrogenic substance followed by 400 bird units of lactogenic substance (given twice daily over a period of five days) Mammary secretion (lactation) occurred

sequent to bilateral resection of the splanchnic nerves is due to the unopposed action of the vagus nerves. However, Carlson, Boyd and Percy<sup>14</sup> found that stimulation of the vagus nerve produces a motor response if gastric tonus is low and an inhibitory response if it is high. McCrea, McSwiney and Stopford<sup>15</sup> also concluded that the primary effect of stimulation of the vagus is dependent on the existing condition of the peripheral mechanism of tonus. Either inhibition or augmentation of gastric tonus may result. Hence, the type and duration of motility depend largely on the degree of gastric tonus exhibited on the day of observation.

In some instances, dogs with the splanchnic nerves sectioned showed no greater tonus and no greater rate and persistence of contractions than did the dogs with these nerves intact.<sup>9</sup> These observations are in keeping with our findings. In certain experiments we observed that gastric motility was more persistent during the control period. Carlson's explanation for this is that section of these nerves eliminates one of the least important of the factors involving the motor activity of the empty stomach. The conditions influencing the stomach through the blood<sup>16</sup> and through the vagi are still subject to practically the same variations as in the normal subject with the splanchnic nerves intact.

Cannon<sup>17</sup> reported that resection of the splanchnic nerves did not alter the gastric movements in the cat. It is difficult to account for this in view of our findings and those of other investigators.

After resection of the left splanchnic nerves we observed that gastric motility was at times continuous throughout a period of observation of from four to five hours. There was also an augmentation in gastric tonus but no appreciable change in the duration of and the interval between contractions. Gastric tetany was frequently observed. After resection of the right splanchnic nerves, the results simulated closely those observed subsequent to the first operation. The periods of activity were equally persistent.

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14 Carlson, A. J., Boyd, T. E., and Percy, J. F. Studies on the Visceral Sensory Nervous System. Innervation of the Cardia and the Lower End of the Esophagus in Mammals, *Am J Physiol* **61** 14, 1922, Studies on the Visceral Sensory Nervous System. Reflex Control of the Cardia and Lower Esophagus in Mammals, *Arch Int Med* **30** 409 (Oct) 1922.

15 McCrea, E. D., McSwiney, B. A., and Stopford, J. S. B. Effect on the Stomach of Stimulation of the Peripheral End of the Vagus Nerve, *Quart J Exper Physiol* **15** 201, 1925.

16 Luckhardt, A. B., and Carlson, A. J. On the Chemical Control of the Gastric Hunger Mechanism, *Am J Physiol* **36** 37, 1914.

17 Cannon, Walter B. Motor Activities of the Stomach and Small Intestines After Splanchnic and Vagus Section, *Am J Physiol* **17** 429, 1906.

EFFECT OF LACTOGENIC SUBSTANCE ON THE MAMMARY GLANDS  
OF MENSTRUATING WOMEN

Liquefaction of the periductal fibrous tissue and shedding of the epithelial elements were observed microscopically in the breasts of monkeys after injections of lactogenic substances<sup>11</sup> Like injections were given menstruating women who had various forms of chronic mastitis but who had not been recently delivered The studies differed, therefore, from those which had previously been made In two instances a biopsy of tissue from the breast was made both before and after the injections, and in three cases, after the injections had been given In all, fourteen women received injections Mammary secretion occurred in three after injections of estrogenic substance<sup>11</sup> and lactogenic substance No secretion was noted in six patients who received estrogenic and lactogenic substances

TABLE 1—*Administration of Estrogenic and Lactogenic Substances with the Production of Mammary Secretion*

Case	Patient	Age, Years	Previous Pregnancy	Diagnosis	Estrogenic Substance		Lactogenic Substance	
					Dose, Rat Units	Total Rat Units	Dose, Bird Units	Total Bird Units
1	M P *	30	1 (10 yrs )	Adenosis	500 every 4th day	3,500	100 daily for 5 days	500
2	M L H	40	1 (23 yrs )	Adenosis	500 every 4th day	3,500	50 twice daily for 7 days	1 120
3	A B N †	40	1 (10 yrs )	Adenosis	500 every 4th day	3,000	100 twice daily for 3 days	600

\* Two biopsies were made three and eleven days after the onset of the secretion

† Two similar courses of estrogenic and lactogenic substances were given in September 1934 and in January 1935, but no secretion was produced The third course, noted above, was given in April 1935

Five of the women who were given only lactogenic substance had no secretion A Negro with gynecomastia and a Negress who had hyperthyroidism received both estrogenic substance and lactogenic substance, but neither showed any evidence of mammary secretion (tables 1 to 3)

This is a small series, but the results indicate that the injection of lactogenic substance may cause mammary secretion in nonpregnant women when they have been previously stimulated with estrogenic substance In the three cases in which secretion was noted (table 1) from 3,000 to 3,500 rat units of estrogenic substance (from 24,000 to 28,000 international units) was administered In each instance estrogenic substance was given intramuscularly before the menstrual period,

<sup>11</sup> Drs J F Anderson and J A Morrell, of E R Squibb & Sons, supplied the estrogenic substance (amniotin) and the lactogenic substance (prolactin) used in these studies

## CONCLUSIONS

Bilateral resection of the splanchnic nerves was performed on a patient with severe diabetes. Observations on the gastric motor mechanism revealed that after bilateral resection of the splanchnic nerves there ensued (1) hypermotility of the empty stomach as observed by the balloon method, (2) an augmentation of gastric tonus, (3) an increase in the amplitude of contractions, and (4) no untoward gastrointestinal symptoms.

and the injections were discontinued during menstruation. Injections of lactogenic substance were started the day after menstruation ceased and were given intramuscularly within a week, the amount given ranging from 600 to 1,120 rat units at the time secretion appeared.

The appearance of secretion was preceded by a feeling of engorgement and heaviness of the breasts and accompanied by an increase in their size. The secretion was creamy white and in no case lasted longer than three days. No more than 10 or 12 drops could be expressed from the nipple at any time. In two cases secretion was obtained from both breasts, and in the third case, from the left breast only. Secretion ceased spontaneously in all cases. Cessation of the secretion occurred in two cases even when lactogenic substance was administered after the secretion appeared and the nipples were stimulated by the patient. In one

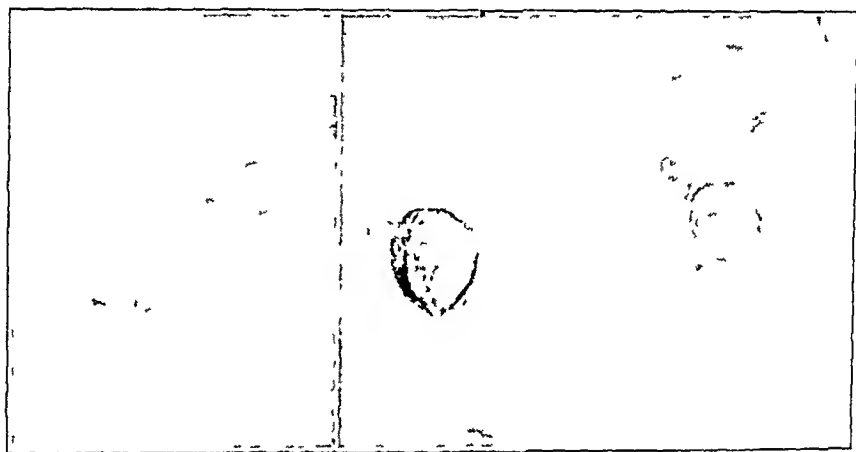


Fig 3 (case 1, table 1) —Photomicrograph of mammary secretion obtained after the patient had received 3,500 rat units of estrogenic substance, followed four days later by 800 bird units of lactogenic substance (160 bird units once daily for five days)

case the breast pump was used, but the period of secretion was not prolonged. In this case two courses of injections of lactogenic substance similar to those given in the third course had been administered seven and four months before without resulting in the appearance of secretion.

Microscopically (fig 3) the secretion in all the cases resembled colostrum, fatty droplets and desquamated cells being found. In case 1 (table 1) a biopsy was performed on the third day after the appearance of the secretion, and another biopsy of tissue from the opposite breast was made eleven days after the secretion first appeared. Microscopic examination of the tissue revealed hypertrophy and an increase in the number of cells lining the lactiferous tubules and an increase in the

crop of the pigeon as a method of bio-assay opened new fields for the investigation of the physiology and pathology of lactation in human beings

Kurziok and his associates<sup>7</sup> have reported on the clinical use of lactogenic substance in thirty-seven women who had been delivered of normal children. Twenty-nine of these women were thought to have insufficient milk. Twenty-one of these showed an increase in the amount of milk after the sixth day post partum, when from 75 to 400 birds units of lactogenic substance was injected intramuscularly. In four of the eight remaining women only a moderate response was noted, and in four no response was observed. In eight normal women in whom the secretion was normal, no response was noted after the use of the lactogenic substance.

Werner<sup>8</sup> gave injections of lactogenic substance (200 bird units daily for from four to fourteen days) to ten castrated women, ranging in age from 21 to 35 years. The breasts were prepared by injections of estrogenic substance to which was added the gonadotropic factor from the urine of pregnant women or progestin in eight cases. All noted enlargement or engorgement of the breast which might be regarded as suggesting the onset of lactation. Lactation did not occur, however, in any case. Anaphylactic reactions were noted in three.

In an experimental study in which an attempt was made to reproduce cystic disease and benign tumors of the breast (Geschickter, Lewis and Hartman<sup>9</sup>) injections of estrogenic substance followed by injections of lactogenic substance were given to four male monkeys and one female monkey. Secretion occurred in the female but not in the males (fig. 1). The female was an adult menstruating macacus and had received 500 units of estrogenic substance followed by the injection of 400 units of lactogenic substance over a period of five days.

Allen, Gardner and Diddle<sup>10</sup> were able to produce lactation in five mature female monkeys by injecting lactogenic substance. Two of these animals had had previous injections of estrogenic substance.

7 Kurziok, R., Bates, R. W., Riddle, O., and Miller, E. G., Jr. The Clinical Use of Prolactin, *Endocrinology* **18** 18, 1934.

8 Werner, A. A. Experiment to Produce Lactation in Castrate Women, *Endocrinology* **19** 144, 1935.

9 Geschickter, C. F., Lewis, D., and Hartman, C. G. Tumors of the Breast Related to the Oestrin Hormone, *Am. J. Cancer* **21** 828, 1934.

10 Allen, E., Gardner, W. U., and Diddle, A. W. Experiments with Theelin and Galactin on Growth and Function of the Mammary Glands of the Monkey, *Endocrinology* **19** 305, 1935.

amount of periductal connective tissue Both these changes (on the basis of work previously reported) may be interpreted as response to estrogenic substance In addition, maturation and secretory activity in the epithelium of the lobules, accumulated secretion and desquamated cells within the lumens were noted These changes, together with the



Fig 5 (case 3, table 2) —Photomicrograph of a specimen obtained for biopsy after the injection of 5,500 rat units of estrogenic substance The tissue was removed in conjunction with an exploration for dilated ducts beneath the nipple Note the hypertrophy and dilatation of the terminal tubules and the periductal hyperplasia Secretion is seen in the lumen

loose, edematous appearance of the periductal tissue, were interpreted as having been caused by the injections of lactogenic substance They were noted in both biopsy specimens, although there had been no demonstrable secretory activity for eight days preceding the last biopsy These



Fig 2—Photomicrographs of specimens from the breast of a male monkey on the sixth day (A) and on the twenty-third day (B) after a course of ten injections of lactogenic substance given twice daily for a period of five days. The monkey had been previously subjected to experimental gynecomastia by injections of 2200 rat units of estrogenic substance over a period of six weeks.



The lactogenic substance in these cases was given in small amounts (40 to 320 bird units), except in two cases. In the case in which 5,000 rat units of estrogenic substance and 720 bird units of lactogenic substance were given (case 2 table 2) the lactogenic substance was administered on'y every third day over a period of seventeen days, and an interval of three weeks elapsed between the last injection of estrogenic substance and the first injection of lactogenic substance. In the case in which 320 bird units of lactogenic substance was given (case 3, table 2) the lactogenic substance was given at the same time as the estrogenic substance. A biopsy was made before and after the injections. Microscopically some evidences of secretory activity were noted. In case 6 (table 3) no secretion was observed, although 2,000 rat units of estrogenic substance and then 780 bird units of lactogenic substance were given.

In the patient with gynecomastia a blood test showed the presence of the estrogenic substance, and a biopsy was made before and after the injections. This patient received 200 bird units of lactogenic substance between April 18 and April 25, 1,000 rat units of estrogenic substance on April 25 and 320 bird units of lactogenic substance between April 26 and May 26. The breast became enlarged and tense, but no secretion was noted (figs 7 and 8).

Rather large doses of lactogenic substance (320 to 740 bird units) were given to women during the menstrual cycle, when supposedly normal amounts of estrogenic substance should be present, but no mammary secretion was noted. Five women had normal menstrual cycles, and injections of lactogenic substance were made on successive periods of seventeen, seven and four days, respectively. In case 1 a biopsy was made before and after the course of injections (fig 9).

Although true functional lactation was not observed, the secretory activity obtained with estrogenic and lactogenic substances indicates that lactogenic substance represents the hormone of the anterior lobe of the pituitary body which stimulates human mammary secretion. This is also suggested by bio-assays of fluid obtained from blue dome cysts in patients with chronic cystic mastitis. In many cases of cystic mastitis a substance may be found which when injected into pigeons produces a typical response in the crop. This response is identical with that obtained after injections of lactogenic substance which has been prepared from beef pituitary glands (beef pituitary glands were the source of the lactogenic substance used in the investigations forming the basis of this report). Further evidence is supplied by the results obtained by Kurziok,<sup>7</sup> which showed an increase in the lactation of women post partum in response to injections of lactogenic substance. The failure of Werner<sup>8</sup> to secure secretion in his series of castrated women was

TABLE 2—Administration of Estrogenic and Lactogenic Substances Without the Production of Mammary Secretion

Case	Patient	Age Years	Previous Pregnancies	Diagnosis	Estrogenic Substance		Lactogenic Substance	
					Dose, Rat Units	Total Rat Units	Dose, Bird Units	Total Bird Units
1	M T*	38	None	Fibro adenoma	700	700	20 twice daily for 5 days	200
2	J D†	13	None	Virginal hypertrophy	1 000 weekly for 7 wks	7 000	120 every 3d day	720
3	P L‡	42	1 (7 yrs)	Dilated ducts beneath nipple	500 daily for 5 days	2 500	50 twice daily for 4 days	320
4	D B	35	None	Virginal hypertrophy	500 twice monthly for 3 mo.	3 000	40 once	40
5	M T	25	None	Fibro adenoma	1,000 once	1,000	60 daily for 5 days	300
6	M J	29	1 (7 yrs)	Virginal hypertrophy	1 000 twice	2,000	60 daily for 10 days	720
7	M W* male	18		Gynecomastia	1 000 once	1 000	20 twice daily for 5 days prior to injection of estrogenic substance, 40 daily for 8 days after injection of estrogenic substance	720
8	L B	25	2 (7 and 9 yrs)	Hyper thyroidism	500 daily for 6 days	3 000	50 twice	160

\* A specimen was obtained for biopsy

† Three weeks elapsed after the last injection of estrogenic substance and the first injection of lactogenic substance

‡ This patient had a previous course of injections of estrogenic substance one month prior to the injections of estrogenic and of lactogenic substance which were given simultaneously. A biopsy was made before the course of these combined injections and another biopsy afterward

TABLE 3—Administration of Lactogenic Substance Without the Production of Mammary Secretion

Case	Patient	Age Years	Previous Pregnancies	Diagnosis	Lactogenic Sub-stance	
					Dose Bird Units	Total Bird Units
1	C S*	49	7	Fibro adenomatous	60 or 40 once daily for 17 days	740
2	E E†	34	1	Cystic disease of breast	50 twice daily for 7 days	420
3	A S‡	36	3	Adenosis	50 daily for 4 days	320
4	I I	26	None	Adenosis	50 daily for 8 days	440
5	L S	21	None	Virginal hyper trophy	50 daily for 6 days	420

\* A specimen was taken for biopsy

† An anaphylactic reaction was observed

‡ This patient was given a course of estrogenic substance two months previously, 500 rat units being given weekly (a total of 2 500 rat units)

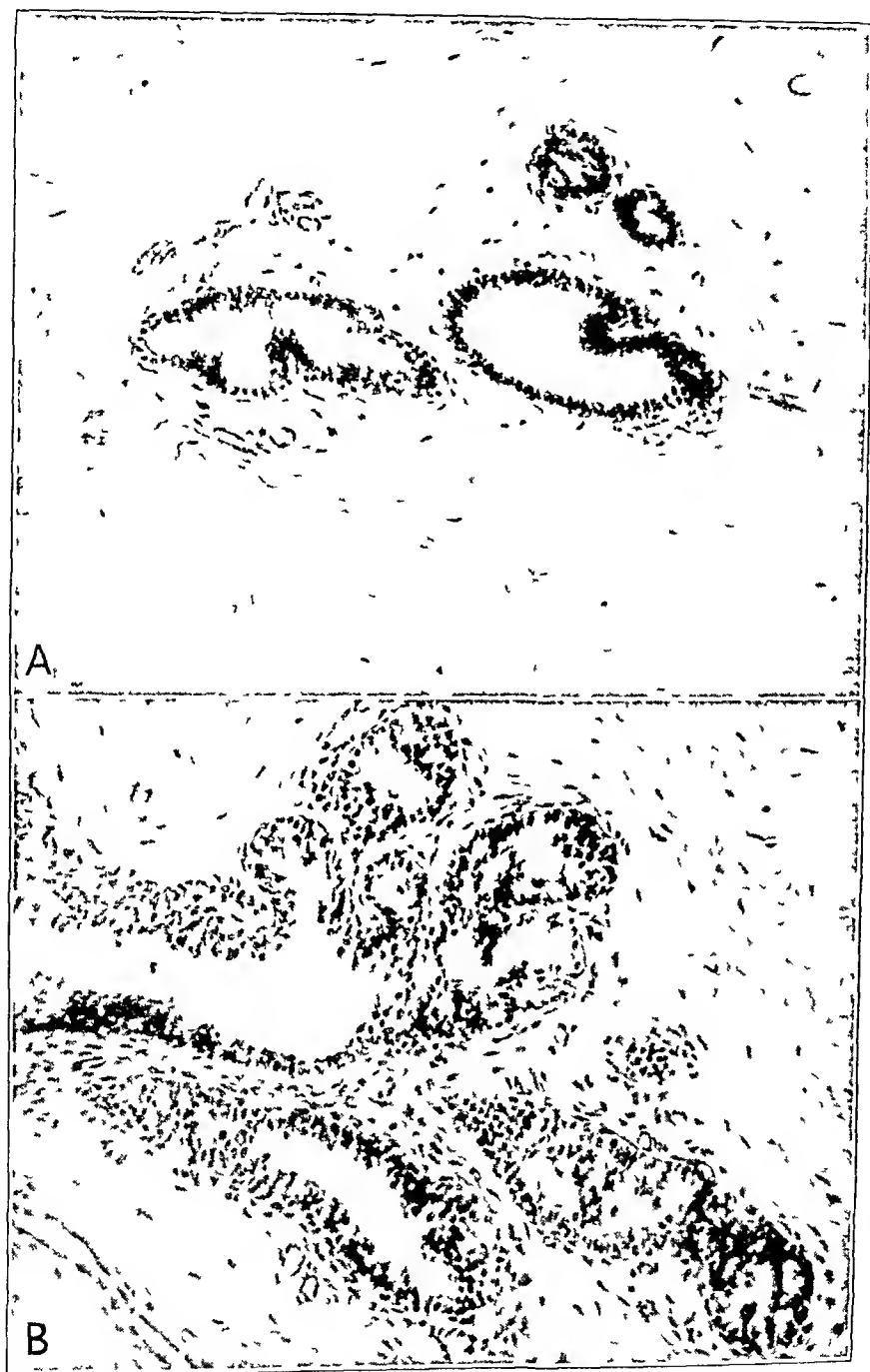


Fig 8—*A*, a specimen taken for biopsy before the injection of lactogenic substance, *B*, after the injections, in the Negro shown in figure 7

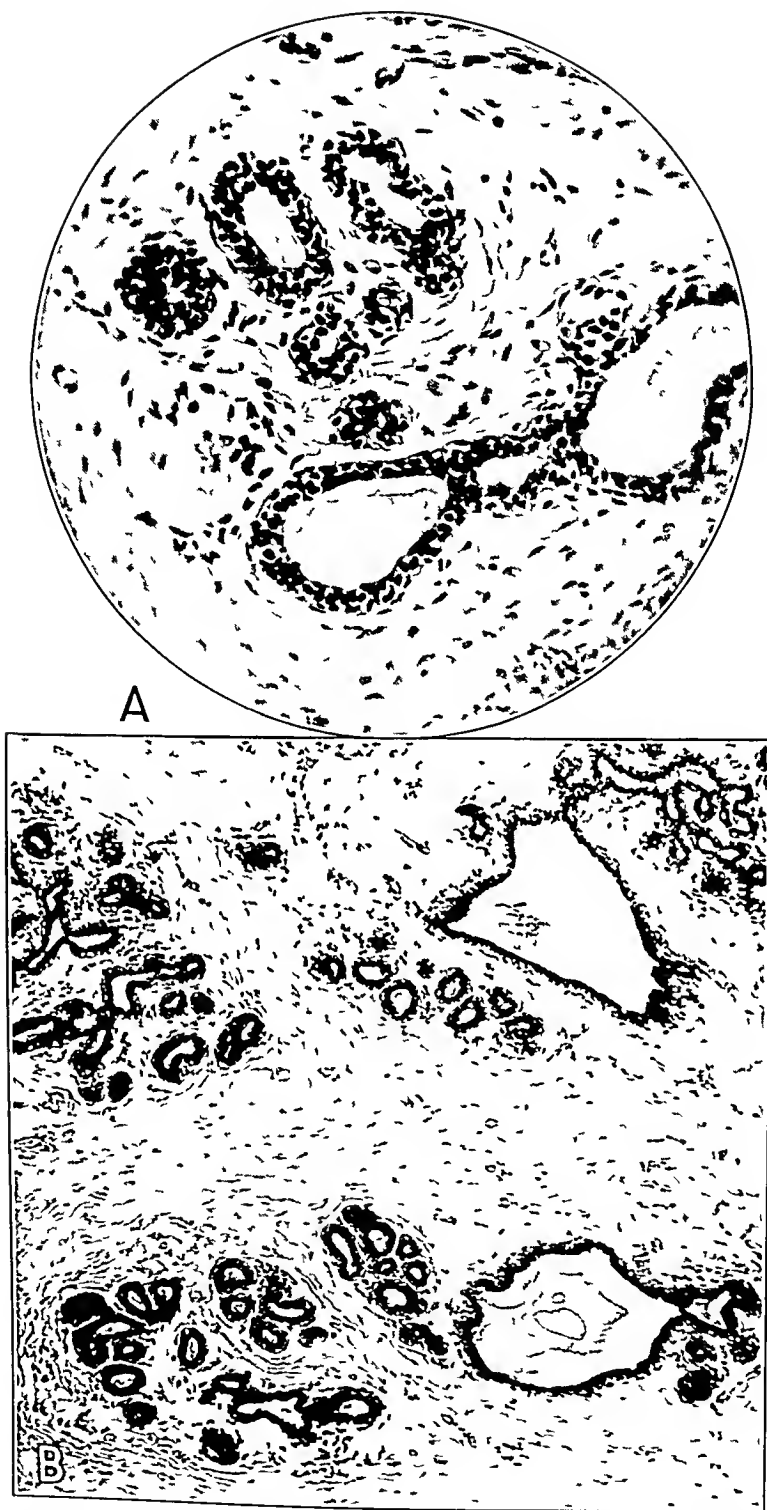


Fig 4 (case 1, table 1) —Photomicrographs of specimens removed for biopsy on the third day (*A*) and on the eleventh day (*B*) after the appearance of mammary secretion. The terminal tubules are dilated and widely separated. Secretion is visible in the lumens of the tubules.

also in the milk mixed with colostrum from lactating cows within the first two weeks of calving. Whole milk obtained at varying periods after an interval of two weeks after calving, however, showed no lactogenic substance. Perhaps the lactogenic substance present in colostrum may play a part in the formation of the witch's milk of nursing infants.

However, it is apparent that lactogenic substance alone or in combination with estrogenic substance does not produce true lactation. Lactogenic substance is not peculiar to lactating animals or to females, since the pituitary glands obtained from castrated bulls (ordinary beef pituitary glands) are a potent source of this hormone. Turner<sup>6</sup> has been able to demonstrate traces of lactogenic substance in the blood and urine of nonlactating cows. Both estrogenic substance and lactogenic substance can be demonstrated in the breasts of human females with chronic cystic mastitis, which is particularly frequent in childless women. The rôle which these hormones may play in the causation of cystic disease is discussed subsequently.

The fact that mammary secretion was stimulated by injections of estrogenic and of lactogenic substance in the three cases listed in table 1 does not indicate that these two hormones alone are sufficient for lactation or the secretion of colostrum. In all three of the patients the breasts were under the influence also of progesterin, a hormone from the corpus luteum. These patients had the form of chronic cystic mastitis which we<sup>13</sup> have termed adenosis, in which the breast is under the influence of increased stimulation by progesterin. This is manifested pathologically by proliferation of acinar elements and minute papillomas, which is characteristic of all cases of adenosis. The administration of estrogenic and lactogenic substances in these cases apparently completes the physiologic cycle and causes mammary secretion.

These studies therefore suggest that both estrogenic substance and progesterin are essential in the preparation of the human breast before an adequate response to lactogenic substance can occur. It is to be noted, however, that lactogenic substance was not effective when given simultaneously with estrogenic substance.

There is additional evidence for concluding that large amounts of both hormones when present simultaneously may be antagonistic in their influence on the breast. In treating women with blue dome cysts of the breast or with galactorrhea which has been present for years it has been found that the administration of large doses of estrogenic substance (1,000 rat units administered every other day for a period of two weeks) will inhibit the secretory activity of the breast and in some instances will cause the disappearance of the palpable cyst. Moreover, in assaying

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13 Lewis, D., and Geschickter, C. F. Ovarian Hormones in Relation to Chronic Cystic Mastitis, *Am J Surg* 24: 280, 1934.

changes were noted also in case 3 (table 2) after injections of estrogenic and lactogenic substances, although there had been no evidence of mammary secretion and no milk could be expressed from the nipple (figs 5 and 6)

True lactating acini were not observed, although serial sections were made. Evidences of secretory activity seemed to be confined to the terminal tubules of the rudimentary acini, which were dilated and widely separated by the edematous periductal connective tissue. It is possible that scattered functioning acini were responsible for the secretion but were not included in the tissue removed for biopsy.

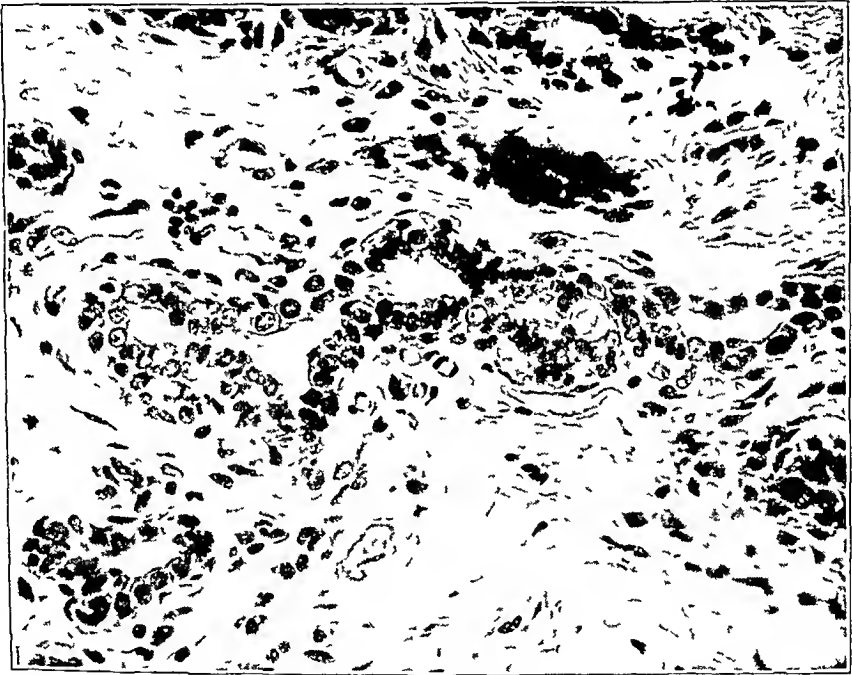


Fig 6 (case 3, table 2)—Photomicrograph of tissue obtained for a second biopsy, approximately six weeks after the tissue shown in figure 5 was removed. During the five preceding days the patient had had daily injections which constituted a total dose of 2,500 units of estrogenic substance and 320 bird units of lactogenic substance.

Large doses of estrogenic substance with smaller doses of lactogenic substance or lactogenic substance given weeks after estrogenic substance had been administered failed to produce definite gross secretion. In the group of cases in which estrogenic substance in amounts varying from 500 to 5,000 rat units (4,000 to 40,000 international units) was given intramuscularly there were six females who were known to have conditions of the breast of the type associated with an increased amount of the estrogenic principle (fibro-adenoma, vaginal hypertrophy).

in some cases by the use of estrogenic substance alone, judging by the twenty patients treated with estrogenic substance only. In the patients who received estrogenic plus lactogenic substance the results noted from six to eighteen months after the cessation of therapy were more striking than those in the patients who received estrogenic substance only.



Fig. 10—Photomicrograph showing epithelial hypertrophy, cyst formation and secretion in a case of cystic disease of the breast. The pathologic process resembles pseudolactation with colostrum formation.

On the basis of results obtained thus far, large doses of estrogenic substance alone are worthy of trial to control the formation of cysts in patients with cystic disease of the breast, and the administration of estrogenic substance plus lactogenic substance is indicated in cases of adenosis.

probably due to depletion of the estrogenic substance in the tissues. Judging from the results obtained for castrated rats, far more estrogenic substance (about fifteen times as much) is needed to prepare the breast for lactogenic substance in castrated women than in noncastrated women. The maximum dose used by Werner was 13,200 rat units. The dose calculated on the basis of the present series for castrated women is in the neighborhood of 45,000 or 50,000 rat units. Moreover, in these women there is a similar depletion of progesterin, which probably is not compensated for by the small injections given in two cases in Werner's series.

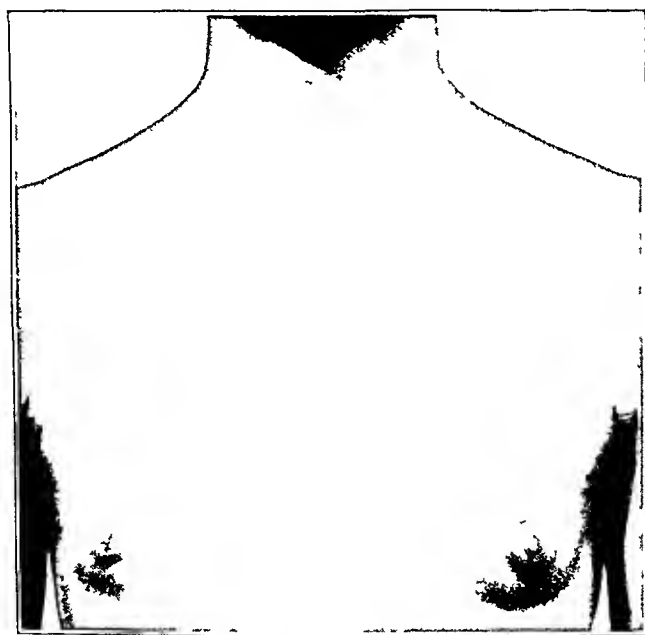


Fig 7—This Negro with gynecomastia received a course of injections consisting of 200 bird units of lactogenic substance for a period of five days, 1,000 rat units of estrogenic substance on the sixth day and 320 bird units of lactogenic substance during the next fifteen days.

Lactogenic substance can be demonstrated both in the mammary tissue and in the colostrum of normal lactating cows. We have assayed the udders of lactating cows in three instances<sup>12</sup>. Two of the animals were killed ten days and one was killed two days after the last milking. In all three instances the extract prepared from udder tissue showed the presence of lactogenic substance when tested on the crops of pigeons. We have been able to demonstrate the presence of lactogenic substance

<sup>12</sup> Dr and Mrs George O. Gev, of this laboratory, cooperated in the extraction of udders and colostrum for lactogenic substance.



## BIO-ASSAY FOR LACTOGENIC SUBSTANCE IN CASES OF CYSTIC DISEASE OF THE BREAST

With regard to cystic disease of the breast, which is a relatively common condition in childless women approaching the menopause, a serous or milky discharge was observed in 3 per cent of a series of five hundred patients studied in this laboratory. The content of such cysts at operation or aspiration usually reveals a cloudy or milklike fluid. Microscopic examination of the excised mammary tissue surrounding the blue dome cyst shows pathologic changes which may closely simulate physiologic lactation (fig 10).

Because of these findings we have assayed cyst fluid and mammary tissue obtained from patients with cystic disease and have found that they contain estrogenic and lactogenic substances (table 4). These assays show that the cloudy milklike fluid may contain high concentrations of these substances (lactogenic substance up to 2,000 bird units per liter and estrogenic substance up to 6,000 rat units per kilogram, fig 11). The fluid from a single cyst, however, with one exception has not been found to contain both hormones. In view of the fact that a similar milklike secretion can be obtained by the injection of estrogenic substance and lactogenic substance in menstruating women, it seems reasonable to conclude that these hormones are responsible for the pathologic secretion observed in cases of cystic disease.

We have assayed the mammary tissue of patients with cystic disease for lactogenic substance with positive results in one case. In view of the fact that this hormone has been obtained by us from the mammary tissue of cows and that by bio-assays we have found estrogenic substance in the mammary tissue of four patients with cystic disease, it seems reasonable to conclude that the pathologic changes observed in the surrounding tissues as well as the secretory changes are the result of stimulation by the estrogenic and lactogenic hormones (fig 12).

## SUMMARY

A series of sixteen patients treated with intramuscular injections of estrogenic and lactogenic substances has been studied.

Mammary secretion was observed in three menstruating women for whom a clinical diagnosis of adenosis of the breast was made and each of whom received approximately 3,500 units of estrogenic substance over a period of a month, followed by injections of from 600 to 1,120 bird units of lactogenic substance given within a week. The secretion ceased within a period of three days and could not be prolonged by further injections or by mechanical stimulation.

Histologic studies of tissue removed for biopsy were made before and after the injections of several cases. The changes of true functional lactation were not observed histologically.



Fig 9 (case 1, table 3) — *A* tissue from a woman with fibroadenoma of the breast after four injections of lactogenic substance. *B* a biopsy specimen obtained one month later from the opposite breast after daily injections of lactogenic substance over a period of seventeen days, making a total of 740 bird units.

# DISTURBANCES IN GASTRO-INTESTINAL FUNCTION AFTER LOCALIZED ABLATIONS OF CEREBRAL CORTEX

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AUGUSTA, GA.

The great difficulty of keeping the totally decorticated animal in a state of suitable nutrition led us to suspect an intrinsic derangement of digestion. It was observed that operations on the frontal lobe were followed by an especially high mortality rate occurring during the third and fourth postoperative weeks. Observation of the function of the stomachs of such animals by previously made fistulas appeared to point to a disturbance of gastric motility. A thorough study of a "chronic" decorticated dog pointed toward evidence of deranged autonomic function. The present series of observations represents an attempt to investigate the phenomena of gastric motility after injury to cortical tissue of the frontal lobe by the use of the Cannon technic of direct visualization with the fluoroscope.

## MATERIAL AND METHODS

Because of the carefully estimated normal standards of Cannon the cat was chosen as the experimental animal. After a variable period of preliminary observation to assure ourselves that the functions of the cats chosen for the experiment fell within the limits of variations to be expected in a normal population, the animals were subjected to localized lesion of the cortex. The case of the brain was opened, the dura was incised and the cortical tissue was removed with a curet. In order to be certain that the surgical procedure in itself was not a factor in producing the results obtained, cortical tissue other than from the frontal lobe was removed in control animals. As a check on the housing, feeding and incidentals as well as on the effect of repeated barium sulfate meals and exposure to roentgen rays, intact animals were also used as controls. The examination of the animals operated on followed the procedure of Cannon for fluoroscopic visualization of gastro-intestinal movements.

## EXPERIMENTAL RESULTS

As an examination of the graphs in figure 1 indicates, there was an increase in intestinal activity beginning shortly after the operation for removal of tissue from

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the fluid recovered by aspiration from untreated blue dome cysts it has been found that while either estrogenic or lactogenic substance may be present in high concentrations, the fluid from a single cyst has not been found to contain both hormones. There was one exception, but in that case the content of estrogenic substance was high and concentration of lactogenic substance was low (table 4).

The treatment of adenosis of the breast in the three cases listed in table 1 by the administration of estrogenic and lactogenic substances

TABLE 4—*Assays of Tissue and Fluid from Patients with Cystic Disease of the Breast for Lactogenic and Estrogenic Substances*

Specimen	Patient	Hormone Assayed	Result of Bio Assay
			Bird Units per Liter
Cyst fluid*	S K	Lactogenic substance	2 000
	L F	Lactogenic substance	720
	Bur	Lactogenic substance	0
	Jar	Lactogenic substance	250
	Car	Lactogenic substance	100
	Gar	Lactogenic substance	750
	N W	Lactogenic substance	250
	Grom	Lactogenic substance	250
			Rat Units per Liter
Cyst fluid†	B C ‡	Estrogenic substance	6,000
	Jar	Estrogenic substance	0
	Car	Estrogenic substance	2,000
	Gar	Estrogenic substance	0
	N W	Estrogenic substance	0
			Rat Units per Kilogram
Mammary tissue	N B	Estrogenic substance	6 000
	R C	Estrogenic substance	1,000
	P D	Estrogenic substance	200
	I D	Estrogenic substance	4 000
	Bro	Estrogenic substance	0
	A I	Estrogenic substance	0
	Bur	Estrogenic substance	0

\* Tested by the response in the crops of pigeons (Riddle test)

† Tested by vaginal smear in castrated rats (Allen Doisy test)

‡ Fluid was removed from cysts of both breasts of this patient. The milky fluid from the right breast contained 6 000 rat units of estrogenic substance per liter. The yellow turbid fluid from the left breast did not contain estrogenic substance.

resulted in the cure of two of the patients and marked improvement in the third for a period of more than a year after the cessation of treatment. The breasts were painful before menstruation and contained multiple indefinite nodules and usually one or more caked areas. They became less painful and lumpy after injections of estrogenic substance (1 000 rat units twice weekly). Patients with this condition, who are usually apprehensive and underweight and often have a palpable thyroid gland, are markedly benefited by treatment with estrogenic substance, but there is difficulty in maintaining this marked clinical improvement.



Fig 2—The stomach of animal 5 opened posteriorly, showing the areas of ulceration. The ulcers are arranged chiefly on the lesser curvature. The photomicrographs shown in figures 3 and 4 are made from the triangle-shaped ulcer near the middle of the lesser curvature.



Fig 3—Photomicrograph of the ulcer mentioned in the legend of figure 2. Laterally, intact mucosa is observed. In the center, a tuft of necrotic tissue is surrounded by a circular depressed ditch. External to the muscular coat is a somewhat thickened artery.

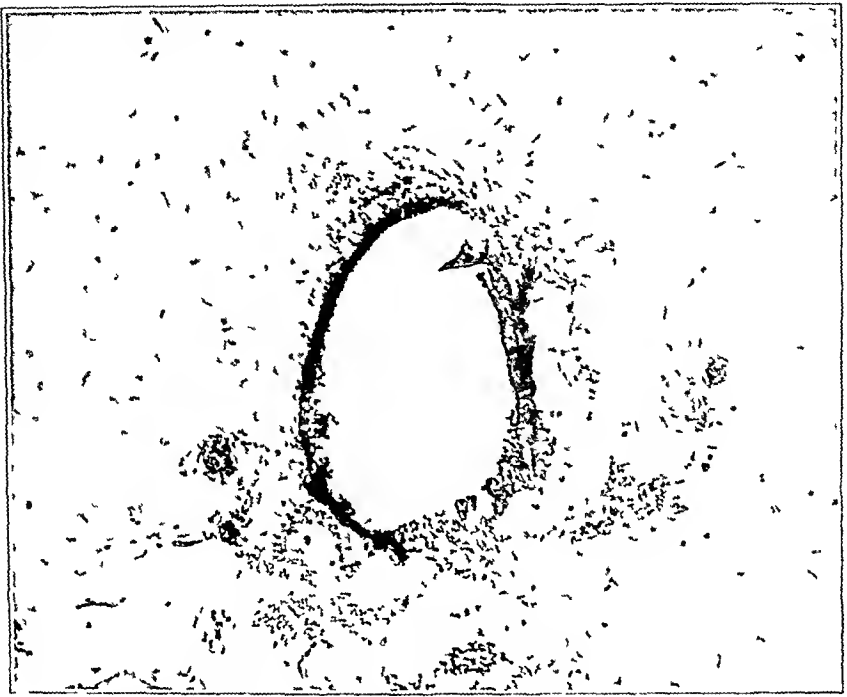


Fig 11—Photomicrograph of tissue from the wall of a blue dome cyst The fluid from the cyst was assayed for lactogenic substance and contained 2,000 bird units per liter

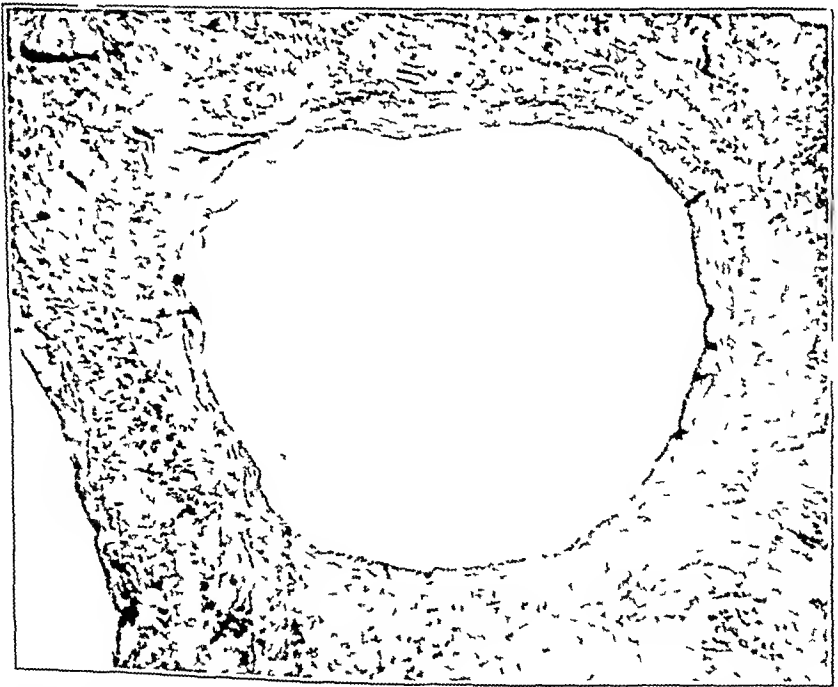


Fig 12—Photomicrograph of tissue removed from a patient with cystic disease of the breast Assay for estrogenic substance showed 6,000 rat units per kilogram of tissue

intestinal activity Watts<sup>2</sup> recently reported similar observations. Watts, in addition, concluded that extirpation of both premotor areas affects gastro-intestinal motility, but his presentation of experimental observations mentioned only stimulation. Stimulation experiments are open to the criticism that the current may spread to the hypothalamus. Watts apparently was relying for his evidence of the effect of extirpation on the finding of intussusception in monkeys from which the premotor area had been ablated (Watts and Fulton<sup>3</sup>). There can be no doubt of the value of the latter finding, which points strongly to the frontal lobe as important for gastro-intestinal motor function. The idea of neurogenic ulcers is of course not new, Keller,<sup>1</sup> following the lead of the Cushing school, reported the experimental production of ulcers after injury to the brain stem. In our animals, however, not only was there no injury to the hypothalamus, but injury of very small parts of the frontal lobe alone (fig 1, no 4) was sufficient to cause ulceration (fig 2). It is not unlikely that the mechanism of production of the phenomena described in this paper is composed of an upper pathway from the cortex to the hypothalamus (such as was described by one of us [F. A. M.<sup>4</sup>] as existing in the ape), an intermediate pathway (such as was described by Beattie, Brow and Long<sup>5</sup> and Krieg<sup>6</sup>) and a terminal autonomic path.

From our observations it would further appear that ulceration is only one phase of a much more extensive disturbance of the gastro-intestinal tract due to autonomic imbalance. We have recently obtained evidence (in one dog) of a postoperative increase in hydrochloric acid in the gastric juice and also of stasis. It is interesting to speculate on the possible reaction of this stasis to the classic thrombotic central artery of a gastric ulcer.

#### SUMMARY

Localized lesion of the frontal cortex of the cat produces a train of events which involves increased activity of the gastro-intestinal tract, at first with increased and later with decreased pyloric tonus. The tone of the cardia, the rate of propagation of the gastric waves, the number of gastric waves present and the number of waves passing in the stomach per minute are also affected. The relaxation of pyloric tone is accompanied by anorexia and succeeded by marasmus and death. Ulcer-like erosions of the gastric mucosa are noted at autopsy in animals with

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2 Watts, J. W. The Influence of the Cerebral Cortex on Gastro-Intestinal Movements, *J. A. M. A.* **104** 355 (Feb 2) 1935

3 Watts, J. W., and Fulton, J. F. *New England J. Med.* **210** 883, 1934

4 Mettler, Fred A. *J. Comp. Neurol.* **61** 509, 1935

5 Beattie, J., Brow, G. R., and Long, C. N. H. *Proc. Roy. Soc., London*, **S. B.** **106** 253, 1930

6 Krieg, W. J. S. *J. Comp. Neurol.* **55** 19, 1932

Bio-assays showed the presence of lactogenic substance in the tissue of udders from lactating cows and in the milk (mixed with colostrum) of lactating cows obtained within two weeks of calving. It was concluded that high concentrations of estrogenic and lactogenic substances and of progesterin are probably essential to normal lactation in the human breast.

The resemblance between the secretory activity seen in patients with chronic cystic mastitis and that obtained in the patients treated in this series has been pointed out.

Bio-assays have demonstrated the presence of estrogenic and of lactogenic substance in the cyst fluid from patients with chronic cystic mastitis. Bio-assays have also shown the presence of estrogenic substance in mammary tissue removed from patients with chronic cystic mastitis.

It is concluded that lactogenic and estrogenic substances play an etiologic rôle in the secretory activity and in the pathologic changes observed in patients with cystic disease.

Dr Charles W. Turner, of the University of Missouri, checked the assays for lactogenic substances.



# ACHOLIC CACHEXIA

## EXPERIMENTAL STUDIES

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AND

EDMUND ANDREWS, M D

CHICAGO

Acholic cachexia, or cachexia cholipriva, is a condition of rapid emaciation terminating fatally which results from complete external drainage of bile. It is indeed astonishing that the prompt fatal outcome of this condition has been recognized only in recent years. Wangensteen's<sup>1</sup> recent review of the older literature revealed a truly astonishing series of statements made by many of the foremost scholars of the last two generations and continuing up to the early 1920's. Such able clinicians as Moynihan,<sup>2</sup> Murphy,<sup>3</sup> Courvoisier,<sup>4</sup> Robson,<sup>5</sup> Deaver,<sup>6</sup> and Balfour and Ross<sup>7</sup> published comments on the apparent innocuousness of complete loss of bile. All believed it was harmless, although Balfour commented on anemia which usually appeared. Bernays,<sup>8</sup> on clinical evidence, stated that "bile is almost if not entirely as much of a secretion as urine."

However, since the decisive series of studies by Whipple and his co-workers, the true conditions have been more clearly understood. One

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1 Wangensteen, O H. Complete External Biliary Fistula. Potential Serious Postoperative Complications, *J A M A* **93** 1199 (Oct 19) 1929

2 Moynihan, Berkley. Essays on Surgical Subjects. Acute Emergencies of Abdominal Disease, Philadelphia, W B Saunders Company, 1921, p 144

3 Murphy, J B, quoted by Ferguson, A H. *Chicago M Rec* **9** 155, 1895

4 Courvoisier, L G. Casuistisch-statistische Beitrage zur Pathologie und Chirurgie der Gallenwege, Leipzig, F C W Vogel, 1890, vol 12, p 293

5 Robson, A W M. Observations on the Secretion of Bile in a Case of Biliary Fistula, *Proc Roy Soc London* **47** 499, 1890

6 Deaver, J B, in discussion on Heyd, C G. Cholecystogastrostomy and Courvoisier Gallbladder, *J A M A* **77** 339 (July 30) 1921

7 Balfour, D C, and Ross, J W. Postoperative Biliary Fistulas, *Arch Surg* **3** 582 (Nov) 1921

8 Bernays, A C. A Successful Case of Ideal Cholecystotomy, with Critical Remarks on the Pathology and the Different Operative Procedures Practiced on the System of Gall Vessels, *Weekly M Rev, Chicago* **12** 350, 1885

the frontal lobe (operations 3, 4, 7, 8, fig 1 and protocols) When the cortical tissue situated posteriorly was removed (no 2 and 5, fig 1), a temporary overactivity was observed, but this soon passed away After the operation there was a disturbance of the number of waves present in the stomach, the rate of propagation of single waves and the number of waves passing per minute This disturbance became more pronounced as time elapsed after the operation Beyond this aggravation with a lapse of time, no clear correlation of these minor irregularities is apparent to us at present Nearly all the animals ate within one hour after the operation

The emptying time of the stomach and the twenty-four hour and forty-eight hour clearance time are fairly constant in the normal animal Shortly after injury to the frontal lobe the emptying time of the stomach was increased This was due to increased resistance to the passage of food through the pylorus and not to gastric hypotonia, since the stomach could be seen to be contracting more vigorously against the resistance of the sphincter

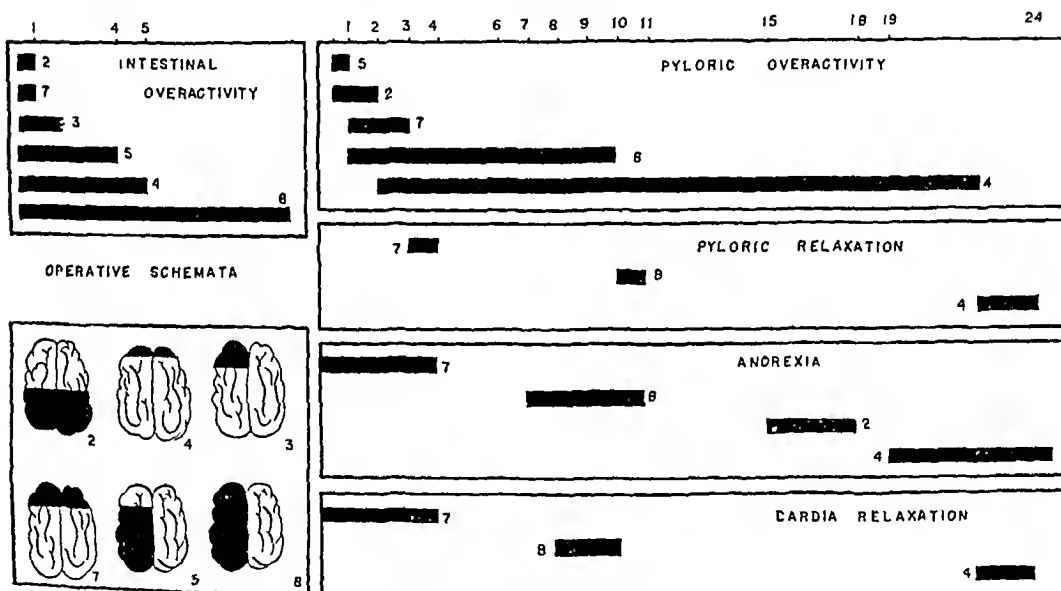


Fig 1—Individual block graphs indicate the observations on cats with damaged cortical tissue The days after operation are indicated by figures across the top of the graphs The section showing intestinal overactivity is based on the rate and amplitude of intestinal movements plus an estimation of the brevity of the intestinal segments The section showing pyloric overactivity is based on the time of passage of the barium into the small intestine and the total emptying time of stomach The section showing pyloric relaxation is based on observations on obvious hypotonus of the pylorus and on the emptying time of the stomach The section showing data on anorexia is based on the failure of the animal to eat the usual diet voluntarily The section on cardia relaxation is based on the observation that the barium would regularly ascend into the esophagus when the stomach contracted, when the animal's movements set up fluid waves or when there was moderate pressure on the abdomen The section marked operative schemata illustrates the extent of the cortex which was removed (black) These observations were verified subsequently at autopsy A resume of the operative procedure on each animal is given in the tabulation preceding the protocols

In the experimental laboratory, the results of establishing external drainage of bile apparently have always been conflicting to a surprising degree. Beginning with Schwann<sup>12</sup> and Bidder and Schmidt<sup>13</sup> nearly one hundred years ago, the operation has usually given a fatal outcome in from two to three months, and it is unnecessary to do more than mention the fact that a bibliography running into hundreds of items might be built up on this subject. On the other hand, in 1882 Rohmann<sup>14</sup> was able to keep such experimental animals in good health for long periods and, backed by rapidly increasing experience with clinical patients, the view that a fatal outcome was sure and that lack of bile in the system was per se a cause of cachexia never seemed to be firmly established.

The reasons for this confusion may be summed up as follows. They have to do mostly with unexpected and unforeseeable technical points in experimental technique.

1 A fistula that leaks bile on the dog's abdominal wall is worthless, as the animals may lick the fistula and thus get sufficient bile to thrive for an indefinite period. Bile, even its own, is apparently quite a delicacy to the carnivorous animal. It is probably the most highly seasoned dish the animal ever encounters. The tendency of the carnivorous animal to eat the liver of its prey first is well known. Even man may acquire a craving for his own bile.<sup>15</sup> Many such cases have been reported, although more often the repulsion is great.

2 The thin-walled choledochus in the laboratory animal has an uncanny power of allowing a ligature to slough through while completely reestablishing its lumen. In the clinic we had long known that veins have such potentialities, but that it is also true in the common duct of the dog was surprising. We have repeatedly seen this happen in a few weeks following operation and, on opening the animals, have found to our astonishment that it was even difficult to tell where the ligature had been placed. It is necessary, therefore, to ligate the duct doubly with silk (not catgut) ligatures and to excise a considerable piece of it.

3 There are frequently abnormal ducts in animals. These tend to lie near the main duct, but at times they are at a considerable distance. It is common in experiments to find that such ducts (which originally must have been almost capillary in size, since for a long period the stools remain free from bile) slowly hypertrophy until a normal bile flow is reestablished. This happens in experiments both in the case of jaundice and in the case of fistulas. Among ten dogs in the series reported on here in which an attempt was made to prolong survival, four had to be discarded after three months for this reason.

4 In long continued experiments with the biliary fistula ascending infection of the bile passage with resulting hepatitis or degenerative changes in the liver, is a complication the avoidance of which is exceedingly difficult. As will be shown in

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12 Schwann, T. H. Versuche um Auszumitteln ob die Galle im Organismus eine für das Leben wesentliche Rolle spielt, *Arch f Anat u Physiol*, 1884, p 127.

13 Bidder and Schmidt, quoted by Rohmann<sup>14</sup>.

14 Rohmann, F. Beobachtungen an Hunden mit Gallenfistel, *Arch f d ges Physiol* 29 509, 1882.

15 Ross, S. G. A Study of Bile Secretion from a Case of Biliary Fistula, *J Lab & Clin Med* 12 1067, 1927.

After a greater or lesser time (depending on the severity of the operation) the animal failed to eat voluntarily, and concomitantly with or shortly after the development of this stage of anorexia the tone of the cardiac sphincter was reduced, so that barium ascended into the esophagus on contraction of the stomach. About this time, or soon after, the condition of increased pyloric tone gave way to a decrease in pyloric tone, which fell far below normal levels. As a result, the emptying time of the stomach was reduced to a phenomenally short time (in some cases to as low as thirty minutes). Although gastric activity was somewhat decreased in this stage, the stomach was still active. In the stage of anorexia and thereafter it was necessary to feed the animals forcibly, and they soon became emaciated and died after considerable loss of weight.

The stomach was seen to be hyperemic and to present petechial hemorrhages if the autopsy was performed within about two weeks after operation. The con-



Fig 4—Photomicrograph of the central raised area shown in figure 3. Note the central artery entering the mucosa. It is seen to contain debris.

gestion was most marked in the vicinity of the cardia. The duodenum also sometimes presented a similar picture of congestion. At later periods ulceration rather than hyperemia was present. The area of ulceration was most marked along the lesser curvature and anterior surface of the stomach (fig 2). The ulcers were punched out and in cross-section (fig 3) showed a circular necrotic moat, in the center of which a somewhat raised tuft of tissue showed a central artery (fig 4), which could be seen to contain debris.

#### COMMENT

That the cortex of the frontal lobe seems to be capable of exerting an effect on gastro-intestinal activity would appear from the work of Keller<sup>1</sup> who stimulated this region and observed changes in gastro-

<sup>1</sup> Keller A D, Hare W K and D'Amour M C. Proc Soc Exper Biol & Med 30 772 1933.

occurred Infection of the liver was often not prevented but simply delayed It makes an ideal method of collecting bile for short periods, especially when a two-way fistula is made and the bile returned to the duodenum when desired

Cholecystonephrostomy, as reported by Kapsinow, Engle and Harvey in 1924,<sup>19</sup> offers many advantages The gallbladder is dissected free from the liver and after being opened is implanted into the right renal pelvis through an opening in the parenchyma The bile is then easily collected with the urine in a metabolism cage The drawback to this method is that complete epitheliation of the tract does not take place and consequently granulating surfaces may persist, as evidenced by pus in the mixed bile and urine While for many purposes such a set-up is ideal, in our hands there was usually profound damage to the liver, and consequently none of our animals in which this was done lived as long as those with simple cannulas often do

More recently Puestow<sup>20</sup> transplanted the section of the duodenum containing the ampulla of Vater on the anterior abdominal wall, with or without cholecystectomy This procedure gives an ideal method of studying the flow of bile under various conditions, and the dogs can be kept alive for indefinite periods if allowed to lick the fistulas For experiments of short duration this method is of great value, but for long ones it is very difficult to collect all the bile and the tendency to lick the fistulas is very great

The apparatus recently devised by Dragstedt and his co-workers<sup>21</sup> for the making of a pancreatic fistula was applied to the gallbladder with singular success The cannula is gold-plated metal with a small flange on the inner end to prevent its slipping out of the gallbladder and on the outer end a threaded tip On this was screwed a sharp spear so that it could be thrust through the abdominal wall, thus assuring a tight fit and preventing the necessity of bringing it out through the operative wound The spear tip was then unscrewed and (fig 1) a metal extension screwed on, to which could be attached a football bladder for collection For use in the gallbladder this was modified slightly, making it longer to permit the necessary access to the dog's rather deeply placed gallbladder and allowing for the ample respiratory excursion of this viscus in the dog The part intervening between the edge of the gallbladder and the abdominal wall was wrapped in omentum The inner flanged end was inserted into the gallbladder through as small a hole as possible without inverting the edges and simply tied in place This apparatus has the disadvantage of not entirely doing away with the action of the gallbladder in concentrating the bile, but as the opening is large and gravity favors rapid drainage, it is evident that the bile never remains in the gallbladder for a very long period This point may be confirmed by reference to the tables, in which it can be seen at once that the analysis showed that the bile was from the liver and did not partake of the character of that from the bladder It is true, however that the secretion of the gallbladder is mixed with the bile, even if the bile does not stay in the viscus long enough to undergo any significant concentration Our success with this type of fistula has been gratifying It has been used in over thirty dogs Nearly 1,500 specimens of bile have been thus

19 Kapsinow, R, Engle, L P, and Harvey, S C Intra-Abdominal Biliary Exclusion from the Intestines Cholecysto-Nephrostomy, a New Method, Surg, Gynec & Obst **39** 65, 1924

20 Puestow, C B The Discharge of Bile into the Duodenum, Arch Surg **23** 1013 (Dec) 1931

21 Dragstedt, L R, Haymond, H E, and Ellis, J C Cannula Gastrostomy and Enterostomy, Surg, Gynec & Obst **56** 799, 1933

long-standing injury, and hyperemia and congestion are to be expected in animals with more recent damage

# PROTOCOLS

A brief resume of the various procedures carried out on each animal is given in the following tabulation

Operation No	Animal No	Operation
2	4	Bilateral removal of the occipital lobe and partial removal of the parietal lobe
3	7	Removal of the left frontal lobe
4	5	Bilateral lesion of the frontal lobe
5	6	Removal of the left parietal occipital and temporal lobes
	3	None
7	7	Removal of the right frontal lobe
8	6	Removal of the left frontal lobe

ANIMAL 3 (female) —An operation was not performed (observations do not appear in figure 1) The animal was kept under conditions identical with those of the other laboratory animals and was repeatedly subjected to feedings of a barium meal and to fluoroscopic examination There was no deviation from normal variations

ANIMAL 4 (male, bilateral removal of the occipital lobe and partial removal of the parietal lobe [fig 1, no 2]) —Slight deviation from normal variations occurred shortly after the operation There was a transitory loss of appetite on the fifteenth day The animal died about two months after the operation of an unknown cause The stomach showed some hyperemia in the dependent portion

ANIMAL 5 (male, bilateral ablation of the frontal pole [fig 1, no 4]) —This animal early showed intestinal overactivity and shortly afterward gave evidence of hypertonus of the pyloric sphincter Nineteen days after the operation anorexia appeared (forced feeding then being instituted) and was succeeded by pyloric relaxation and relaxation of the cardia The animal was killed on the twenty-fourth day The stomach showed ulcer-like erosions

ANIMAL 6 (female, two operations ablation of the left occipital, parietal and temporal lobes [fig 1, no 5] and seven days later removal of the left frontal lobe [fig 1, no 8]) —Early after the first operation intestinal and pyloric overactivity manifested themselves At the beginning of the fourth postoperative day, however, no deviation from normal was apparent Following the second operation the intestinal and pyloric overactivity continued for ten postoperative days Anorexia appeared on the seventh day, and forced feeding was instituted Relaxation of the cardia appeared on the eighth day and pyloric relaxation on the tenth, and the animal died on the eleventh day At autopsy the stomach was red and hemorrhagic and presented small ulcerated areas

ANIMAL 7 (female, two operations ablation of the left frontal lobe [fig 1, no 3] and, seven days later, removal of the right frontal lobe [fig 1, no 7]) —Early after the first operation and during the first two postoperative days intestinal overactivity was observed No further observations were made on this point, and, no other deviations being observed, the animal was again operated on seven days later Following the second operation the animal would not eat spontaneously, and relaxation of the cardia was observed during the first postoperative day Pyloric overactivity was present at the end of the first day, and at the end of the third day pyloric relaxation occurred The animal died on the fourth postoperative day The stomach was hyperemic and was ulcerated near the cardia The antrum was apparently normal The duodenum showed numerous small hyperemic spots

was attained in all dogs reported on. Feedings were begun the day after operation, but usually all the food offered was not consumed until seven or eight days after operation. During the rest of the periods of observation all the food was immediately and avidly consumed.

The diet consisted of 250 Gm of lean meat and 200 Gm of bread. The meat was cooked and then ground with the bread into a homogeneous paste, with the addition of about 500 cc of water per ration. Drinking water was supplied *ad libitum*. One day a week the dogs were given only water. Aliquot samples of each batch of meat were taken for determination of cholesterol. It was found that the cholesterol content of the bread was constant, and therefore each loaf was not tested. The portions were weighed each day in order that the total weight of the food consumed might be calculated and, from this, the cholesterol content in the diet. On this diet the stools were generally formed. As seen in tables 1 to 4, the dogs were put on a diet of raw meat in the latter portion of the period of their survival. Under this regimen attacks of diarrhea occurred, and to control this complication bone ash was occasionally added to the diet.

For the various analyses samples of blood, 30 cc each, were needed, and about twenty were taken over periods of from four to five months—not an insignificant total quantity in relation to the onset of anemia. In the early stages such samples were taken every four days, but later these periods were lengthened to eight days and then to sixteen days, or even longer. Determinations of blood cholesterol were made by the original Bloor method<sup>22</sup>. Tests for fragility were made by the Sanford<sup>23</sup> method, for blood fats by the Bloor<sup>24</sup> method, and for free and bound calcium by Clark and Collip's<sup>25</sup> modification of the Kramer and Tisdall method<sup>26</sup>. The red blood cell counts were made with an ordinary pipet and the hemoglobin estimations by the Sahli scale.

The bile was collected from the bags daily. It was found unnecessary to use precaution to insure sterility. The specimens were put into 2 volumes of alcohol for preservation and pooled for analysis for periods, as shown in the tables. In each instance the football bladder was washed daily, as was the canvas bag in which it was slung about the dog's abdomen. The bile was measured daily and the analysis for bile salts and cholesterol made by a method previously reported by Andrews and Hrdina<sup>27</sup>. The acid content of the bile was estimated by the aminonitrogen method of Schmidt and Dart<sup>28</sup> and expressed as glycocholic acid.

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22 Bloor, W. R. The Determination of Cholesterol in Blood, *J Biol Chem* **24** 227, 1916.

23 Todd, J. C., and Sanford, A. H. Clinical Diagnosis by Laboratory Methods, ed 7, Philadelphia, W. B. Saunders Company, 1931.

24 Bloor, W. R., Pelkan, K. F., and Allen, D. M. Determination of Fatty Acids in Small Amounts of Blood Plasma, *J Biol Chem* **52** 191, 1922.

25 Clark, E. P., and Collip, J. B. A Study of the Tisdall Method of Determination of Calcium of Blood Serum with a Suggested Modification, *J Biol Chem* **63** 461, 1925.

26 Kramer, B., and Tisdall, F. F. A Simple Technic for the Determination of Calcium and Magnesium in Small Amounts of Blood Serum, *J Biol Chem* **48** 339, 1921.

27 Andrews, E., and Hrdina, Leo. A Method for Estimation of Both Bile Salts and Cholesterol in Small Amounts of Bile, *Proc Soc Exper Biol & Med* **29** 1102, 1932.

28 Schmidt, L. W., and Dart, A. E. Estimations of Bile Acids in the Bile, *J Biol Chem* **45** 145, 1920.

of their many significant contributions was the establishment of the fact that although complete external biliary drainage was invariably rapidly fatal it took but minimum amounts of bile administered by mouth or leaking into the intestine through an incompletely occluded choledochus to maintain animals in perfect health for many years.<sup>9</sup> This amount for the dog is distinctly under 5 cc per day per kilogram of body weight. In man it has never been accurately determined but is probably of the same order of magnitude.

With these points in view one can evaluate more clearly the exceedingly contradictory evidence both from the clinic and from the experimental laboratory. From a clinical standpoint, one can see at once that most of the biliary fistulas which were studied originated in stones and strictures of the ducts and hence were as all clinicians well know, incomplete. In the earlier days of surgery cholecystostomy was a common operation. Quite naturally in cases in which the patency of the common duct was not assured at the operation permanent fistulas resulted but that many of these were complete and not partial or even intermittent seems doubtful from the present knowledge. On the other hand it is quite well known to surgeons today that disastrous results follow the establishment of an external biliary fistula in cases of obstruction of the common duct due to carcinoma. Formerly this was frequently done with intent to relieve the jaundice or, as I have heard it expressed "to let the poisonous bile out of the system." Today even the student of medicine knows that with such external drainage of bile the patient already emaciated from starvation and cancerous cachexia seldom survives for even a month. Substituting a complete external biliary fistula in a case of jaundice in order to relieve toxemia has no scientific basis. To our knowledge the dogs which survived the longest with complete fistulas are the two 5½ months old which are reported on in this paper. On the other hand Dostal and Andrews<sup>10</sup> maintained a dog alive for sixteen months with complete jaundice. Most dogs with complete biliary fistulas live less than two months while most with complete jaundice survive for about six. McWhorter<sup>11</sup> in some studies on choledochus cysts called attention to the fact that intermittent and severe jaundice, which is associated with them is not incompatible with long survival while all patients twenty-two in number, in whose cases external drainage was done died.

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9 Queen, F. B., Hawkins, W. B., and Whipple, G. H. Splenectomy in Bile Fistula Dogs, *J. Exper. Med.* **57** 399, 1933.

10 Dostal, L. E., and Andrews, E. Sixteen Months' Survival with Complete Biliary Obstruction in a Dog. *Proc. Soc. Exper. Biol. & Med.* **29** 547, 1929.

11 McWhorter, G. I. Congenital Cystic Dilatation of the Common Bile Duct, *Arch. Surg.* **8** 604 (March) 1924.



TABLE 2.—Data on Dog 958 with an Experimental Biliary Fistula

[illegible]

our results, we have reason to believe that many of the previously reported phenomena usually associated with acholic cachexia are more readily explicable as manifestations of damage to the liver

#### METHODS

It is quite clear, therefore, that the type of experimental preparation used is an important, if not the most important, factor in the study of biliary cachexia. For these reasons it is necessary to review the various experimental set-ups used and to comment on their relative value in experiments planned for various purposes. The objects to be sought are to avoid ascending infection, to prevent damage to the liver and to provide for collection of bile. The simple cholecystostomy with ligation of the common duct has many drawbacks. The gallbladder of the dog is not sufficiently long to reach the skin, and therefore complete epithelialization of the tract is impossible. It usually pulls away, and the gap becomes a tract lined by granulation tissue which not only contaminates the bile for analysis but causes infection. Collection of all the bile from such a fistula soon becomes impossible, and leakage about a tube in the gallbladder usually occurs. The odor and taste of this soon stirs up the dog to attempt to lick or eat his own bile, thus defeating the purpose of the experiment. A plaster collar to prevent the dog's reaching the fistula is only partially successful.

Furthermore, in this type of fistula the gallbladder tends to retract from the skin, and the resulting sinus, although it may be kept patent by the pressure of the bile, becomes very narrow. The result is that the gallbladder remains full of bile and overflows only under pressure. Thus the bile is constantly subjected to the concentrating action of the mucosa of the gallbladder and in composition resembles bile from the bladder much more than bile from the liver.

The insertion of a tube into the common duct with or without accompanying cholecystectomy is a marked advance. Even with this method ascending infection is common, and in our experience there has always been the great drawback that after weeks or months the cannula is very likely to slip out. In experiments intended to last until death from acholic cachexia takes place such a set-up usually results in disappointment at a critical time—the rapid terminal collapse of the animal. In 1923 Rous and McMaster<sup>16</sup> reported a method which seemed to overcome many of these difficulties. They avoided ascending infection from the outside by using a much longer tube than was necessary simply to reach the skin, the extra coils of which were allowed to lie within the abdomen. Thus the liver was placed at a much greater distance from the skin, and hepatitis did not take place. Furthermore the long coils did not favor the pulling out of the tube from its insertion into the duct by accidental trauma. While some workers<sup>17</sup> found that this type of fistula gives very good results, others encountered great technical difficulties<sup>18</sup>. In our experience the preparation usually did not last long enough to enable us to follow a dog through until death. After a few weeks the tubes tended to become clogged with deposits of pigment and calcium, and periods of jaundice

16 Rous, P, and McMaster, P. D. A Method for Permanent Sterile Drainage of Intra-Abdominal Ducts as Applied to a Common Duct, *J Exper Med* **37** 11, 1923

17 Elman, R, and Hartmann, H. F. Spontaneous Peptic Ulcers of Duodenum After Continued Loss of Total Pancreatic Juice, *Arch Surg* **23** 1030 (Dec) 1931

18 Dostal, L. E, and Andrews, E. Etiology of Gallstones. III Effect of Diet on Bile Salt-Cholesterol Ratio, *Arch Surg* **26** 258 (Feb) 1933

TABLE 4—Data on Dog 959 with an Experimental Biliary Fistula

Date	Blood				Bile				Intest.				Food		Comment											
	Body Weight Kg	Red Blood Corpuscles per Cu Mm	Hemoglobin, per Cent	Fragility	Fats Mgr per 100 Cc	Cholesterol, Mgr per 100 Cc	Calcium, Mgr per 100 Cc	Total Output Cc	Daily Output, Cc	Daily Output per Kilogram Cc	Cholesterol		Bile Acids			Total Cholesterol, Mgr	Weight, Gm	Total Choles-terol, Mgr	Weight, Gm	Total Choles-terol, Mgr						
											Average Daily Output Mgr	Total Output, Mgr	Average Daily Output Mgr	Total Output Mgr							Output per Kg Mgr	Bile Acids Cho-lesterol Ratio	Dry Weight Gm per 100 Cc	Cholesterol, Mgr per 100 Cc		
4/20/33	17.5	5,820,000	76	0.42	0.32	166	11.5																			
4/21/33	17.5	7,210,000	77	0.41	0.30	138	23.1																			
4/27/33																										
4/28/33	17	7,730,000	79	0.46	0.34	170	300	11.3																		
4/29/33	16.5	6,320,000	80	0.48	0.34	170	281.5	11.1		978	103	6	11	17	13	19		38	300	114	693	1,960	549	821		
5/1/33	10.5	6,860,000	76	0.46	0.4	88	250	11.3																		
5/11/33	16.7	6,130,000	75	0.40	0.12	115	272	12.1		914	101	6	24	24	219.4	518		77	165	123	970	1,777	776	1,104		
5/15/33	10.7	5,490,000	75	0.46	0.34	93	7260	11.8																		
5/19/33	10.8	6,170,000	73	0.46	0.38	136	270	12.3		1,384	173	10	13	23	181	198		10	150	60	978	1,875	794	1,191		
5/23/33	17	5,930,000	70	0.48	0.40	115	272	10.9		610	152	8.9	20	30	122	140		70	125	98	728	1,577	582	873		
5/25/33	Seven premature pups born (cholesterol estimation on litter)																									
5/27/33	16.0	3,240,000	70	0.40	0.34	115	300	11.1		526	131	7.9	40	52	210.4	341		34	187.5	63	883	1,800	707	1,060		
6/1/33	16	5,100,000	61	0.46	0.40	106	215	11.4		1,223	306	19	50	132	611.5	191		50	100	50	977	758	782	1,173		
6/5/33	15.4	5,750,000	65	0.44	0.36	111	190	11.7		950	277	15	48	113	446	01		46	150	69	770	2,000	600	900		
6/9/33	15.8	4,990,000	70	0.44	0.34	104	181	11.8		692	173	10.9	40	69	276	196		55	187.5	106	1,000	2,600	800	1,100		
6/13/33	15.8	4,170,000	73	0.48	0.40	130	176.4	10.8		593	173	8	60	79	321.8	179		117	102.5	119	750	1,700	600	810		
6/21/33	15.5	4,970,000	78	0.48	0.34	120	150	9.3		1,232	308	19	8.5	26	101.7	283		133	215	285	1,750	2,445	1,400	1,890		
6/29/33	15.4	5,780,000	77	0.48	0.32	97	142.8	10.2		1,420	140	9	23	32	237	366		163	95	151	1,750	3,758	1,400	1,890		
7/7/33	15.2		65	0.16	0.32	109	136	10.7		1,070	136	8.9	14.1	19	178.6	289		260	105	129	1,750	2,434	1,400	1,890		
7/21/33	15.0	5,600,000	70	0.46	0.32	120	270	10.4		1,615	201	13	10.9	22	176	339		185	115	212	1,500	1,325	2,800	3,780		
8/9/33	13.4	6,320,000	65	0.46	0.34	130	300	10.7		941	55	4	20.7	11	194	340		15	200	210	1,750	4,271	1,400	1,890		
8/24/33	12.6	5,600,000	62	0.44	0.46	107	250	9.3		1,627	120	9.5	24	28	462	285		5,000	5,406	2,400	5,000	5,406	2,400	3,240		
9/1/33	500 Gm raw meat on 8/21/33																									
9/11/33	10.4	6,200,000	68	0.42	0.46	111	193	8.5		1,347	67	6	24	46	323	290		30	79	23	7,500					
9/21/33	10									883	126	12.6	13	16	114.7	247										
Totals										17,965	2,066	174	137.9	716.7	1,228.7	1,000		246		2,772		42,173				
Averages										140		10	25.7	42.1		366		362								

Daily subcutaneous injection of 0.5 cc of viosterol was begun 9/1/33

Dog killed

25.769

collected, and the number of lost specimens is under 1 per cent. In a few cases there was deposit of biliary concretions on the tube to such an extent as to obstruct it partially, but with the knowledge of exactly how long the tube was, it was a very simple matter to insert a probe and scrape this deposit out without damaging the gallbladder. When obstructed, a few drops of bile may appear about the tube, or the appearance of slight jaundice gives warning. The football bladder is slung about the dog's abdomen in a linen bag. The fistula is almost invariably completely dry, and no bile leaks about the outside of the tube. It is perhaps for this reason that we did not find it necessary to put plaster collars on the dogs, as when there is no bile on the skin the tendency to lick or bite the apparatus does not seem to be present.

With the use of this preparation we kept four dogs alive for from four and one-half to five and one-half months, considerably longer than the usual period of survival when other types of fistula are used. The absence of ascending infection in all cases was striking, and the liver did not show the usual damage found in animals with experimental biliary fistulas. As will be seen, this prob-

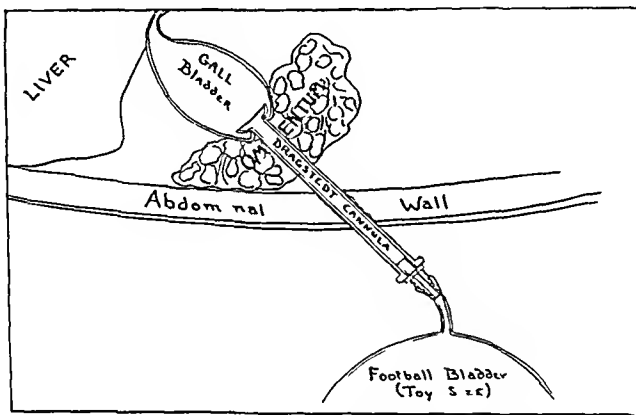


Fig 1—Diagram showing the use of the Dragstedt cannula in the deeply placed gallbladder of the dog. The part intervening between the edge of the gallbladder and the abdominal wall is wrapped in omentum.

ably accounts for the fact that many of the phenomena usually said to be the results of acholic cachexia were not found in our animals.

All these various types of preparations have been used, for the most part in experiments of short duration. In all those designed to last for periods of more than from two to three weeks, the Dragstedt cannula was used. The protocols as well as the results of the various groups of experiments and the comment will be given under separate headings. However, since over one-half of our data were taken from the results obtained on four dogs in which intensive studies were made for very long periods, the protocols of these will be given in detail first. The four large tables are illustrative of these experiments and are included for cross-reference, although for the sake of clarity data from them are sometimes included with other material in smaller tables.

#### PROTOCOLS

Cholecystostomy was performed on dogs under ether anesthesia and the Dragstedt cannula inserted according to the method just described. Primary union

probably due to variations in the intestinal flora, which may or may not cause a fatty acid-containing stool

The volume of the bile excreted varied widely for no apparent reason. The dogs were allowed water ad libitum, and the intake of fluids might have influenced the volume. The average output was from 6 to 20 cc per kilogram of body weight per day. Whipple and his co-workers<sup>30</sup> stated that "variations in bile secretion are startling and inexplicable." Our experience was that when all the bile was drained to the outside the excretion was about one-third less than normal. In this observation Stadelmann,<sup>31</sup> Whipple and his associates<sup>32</sup> and others agreed. The average of our entire series was 10.4 cc per kilogram per day. However, the unexplainable variations<sup>33</sup> were extreme (from 3 to 23 cc per kilogram per day). There was no tendency for the excretion to lessen in the latter periods of extreme cachexia (tables 1 to 4).

In the human being it appears that the biliary excretion is considerably less than this amount per kilogram. Pfaff and Balch<sup>34</sup> got 525 cc per day from a patient with a biliary fistula. Ross<sup>15</sup> found that it varied between 505 and 725, averaging 556. Andrews, Hrdina and Dostal<sup>29</sup> placed it somewhat higher but within the same range. In Ross'<sup>15</sup> observations on one human subject there was an increase of about 50 per cent when bile was fed by mouth. In 1902 Brand<sup>34</sup> reviewed a large series of reports of biliary fistula, and his very extensive analysis showed that the average for man was from 500 to 1,100 cc per day. In his report as in most others the weights of the patients were not given, but if they are taken to average about 70 kilograms, the average excretions would run between 7 and 17 cc per kilogram per day, in most cases being much nearer the lower figure.

Similar violent fluctuations occurred in the quantities of the biliary constituents which were measured (tables 1 to 4). The cholesterol concentration appears to have no relation to that of the bile salts. Similarly the amounts of cholesterol or bile salts excreted appear to have no relation to the concentration of the bile. There is apparently as Wisner

30 Foster, F. M., Hooper, C. W., and Whipple, G. H. Metabolism of Bile Acids. Normal Fluctuation in Healthy Bile Fistula Dogs, *J. Biol. Chem.* **38**: 367, 1919.

31 Stadelmann, E. Ueber das Vorkommen von Gallensauren Hippursäure und Benzoesäure in den Nebennieren, *Ztschr. f. physiol. Chem.* **18**: 380, 1893.

32 Foster, M. G., Hooper, C. W., and Whipple, G. H. Metabolism of Bile Acids. Administration by Stomach of Bile, Bile Acids, Taurine and Cholic Acid to Show Influence upon Bile Acid Elimination, *J. Biol. Chem.* **38**: 379, 1919.

33 Pfaff, F., and Balch, A. W. An Experimental Investigation of Some of the Conditions Influencing the Secretion and Composition of Human Bile, *J. Exper. Med.* **2**: 49, 1897.

34 Brand, J. Beiträge zur Kenntnis der menschlichen Galle, *Arch. f. d. ges. Physiol.* **90**: 494, 1902.

TABLE 1—Data on Dog 940 with an Experimental Biliary Fistula

Date	Body Weight Kg.	Blood					Bile				Bile Acids				Feces				Food		Comment
		Red Blood Corpuscles per Cu Mm.	Hemoglobin, per Cent.	Fragility	Retic. Mls. per 100 Cc.	Cholesterol, Mgs. per 100 Cc.	Total Output, Cc.	Daily Output, Cc.	Bile Output per Bilegram Cc.	Average Daily Output, Mgs.	Total Output, Mgs.	Output per Kg. per Day, Mgs.	Bile Acids Cholesterol Ratio	Dry Weight Gram	Cholesterol, Mgs. per 100 Cc.	Total Cholesterol, Mgs.	Weight, Gram	Total Cholesterol, Mgs.	Weight, Gram		
4/28/23	18.1	6,540,000	80	0.46	0.76	158	240	11.7													(1) Serum jaundiced (2) tetanic convulsions for 15 min. (3) corneal opacity of eye (left)
5/2/23	19.5	6,760,000	78	0.44	0.0	115	207	12.1													
5/5/23																					
5/10/23	19	6,240,000	75	0.44	0.76	158	240	11.7													
5/11/23	18.5	5,100,000	75	0.70	0.70	170	180	11.5													
5/15/23	17.1	6,040,000	70	0.48	0.31	120	201	11.9													
5/16/23	17	4,810,000	70	0.40	0.31	99	168	12.4													
5/21/23	16.8	4,520,000	60	0.44	0.31	100	170	11.3													
5/27/23	15.6	3,920,000	62	0.41	0.40	170	21	13													
6/1/23	15	6,400,000	63	0.41	0.41	111	191	11.7													
6/5/23	10.5	6,710,000	61	0.41	0.31	107	170	11.2													
6/9/23	10.8	4,760,000	78	0.44	0.28	173	176	12.1													
6/13/23	16.2	5,180,000	75	0.46	0.70	111	140	11.1													
6/21/23	16	6,940,000	75	0.40	0.72	99	150	11.7													
6/29/23	15.1	6,400,000	70	0.41	0.72	84	140	9.9													
7/7/23	15.2		61	0.46	0.71	170	142.8	9.8													
7/24/23	11.8	6,860,000	75	0.46	0.70	121	162	10													
8/1/23	11.1	5,970,000	65	0.41	0.31	107	158	9.9													
8/25/23	11.2																				
Totals																					Dof. killed
Averages																					

30.08 Dos. killed

29.967

773

55.1

1,750

29.967

773

55.1

1,750

29.967

773

55.1

1,750

29.967

773

55.1

1,750

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and Balch,<sup>33</sup> Seyderhelm and Tammann<sup>37a</sup> and Baumann<sup>37b</sup> reported clinical cases in which this factor seemed to be important. Balfour and Ross<sup>7</sup> cited one case in which an apparently complete fistula had been present for three years, and except for the fact that the patient's hemoglobin content was 35 per cent no other pathologic lesion was evident. In the one hundred and sixty-six cases reported by them, most of the patients who were cachectic were profoundly anemic. In the light of modern knowledge of the condition it seems reasonable to assume that the patients who were not cachectic had incomplete fistulas. Most of these authors, as well as many others, pointed out that administration of bile by mouth in varying amounts will bring about marked regeneration of the blood. Queen, Hawkins and Whipple<sup>9</sup> demonstrated how little bile is needed to keep an animal in normal health, and from our own experiences we feel inclined to believe that his minimum of 5 cc per kilogram per day represents the upper rather than the lower limits of the average. On two different occasions we noted a sudden gain in weight in experimental animals with apparently complete fistulas. Although in each case it was subsequently shown that the gain in weight was due to a partial reestablishment of the common duct, bile was not evident in the stools, even by chemical tests, for several days.

While it seems the almost unanimous opinion of all workers that the anemia is due either to loss of pigment or to avitaminosis (which will be discussed later), there has been a definite opinion to the contrary expressed by Whipple and his associates<sup>38</sup>. In their experience anemia simply did not occur, provided the dogs were kept in good general condition and provided the fistulas were functioning properly. In their opinion, ascending infection is the most important factor, although intoxication of other sorts and faulty diet may have considerable influence. Some observers have studied the general type of blood picture and found that usually the hemoglobin fell considerably faster than the red count and that in many cases leukopenia was present as well. Lymphopenia has also been noted. These factors are hard to correlate with a picture of chronic septic anemia and suggest that damage to the liver rather than infection may play a rôle.

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37 (a) Seyderhelm, R, and Tammann, H. Ueber die Blutmauserung. Die Gallenfistelanämie des Hundes, *Ztschr f d ges exper Med* **57** 641, 1927. (b) Baumann, W (Gottingen). Ueber die Blutmauserung. Weitere Untersuchungen über die zur Entstehung der Gallenfistelanämie führenden Störungen, *ibid* **75** 401, 1931.

38 (a) Whipple, G H, and Smith, H P. Bile Salt Metabolism. V. Proline, Tryptophane and Glycine in Diet, *J Biol Chem* **89** 705, 1930. (b) Hawkins, W B, Sribhishaj, K, Robschert-Robbins, F S, and Whipple, G H. Bile Pigment and Hemoglobin Interrelation in Anemic Dogs, *Am J Physiol* **96** 463, 1931.







The feces were collected daily and pooled for periods. They were dried, powdered, mixed and weighed and aliquot samples taken. The cholesterol content was determined by the method of Bloor<sup>22</sup>. In most cases the period of ether-alcohol extraction was over six months. Most of the animals defecated only during their periods of exercise. When the stools were liquid, adequate collection was impossible. For this reason our figures on the cholesterol content of the stools are incomplete, probably representing less than half the actual amount passed, as it is well known that the diarrhea stool usually has the highest sterol content.

#### GENERAL OBSERVATIONS

The loss of weight was most rapid in the first month, then the descent was gradual up to a week or two before death, when it again became rapid (fig 2). Often the first rapid loss of weight was in itself fatal, death frequently occurring in the third or fourth week. Whipple stated that such rapid death is due to infection of the fistula, but that was not our experience. It seemed that after the first sudden loss in weight, the dogs began to compensate for the loss of bile. If this compensation broke down, death took place fairly promptly. In some of the dogs which lived for from four to five months there was only a slight loss during the second and third months. On the other hand if one includes the number of dogs dying within the first three to four weeks, the average length of life was probably about five weeks. Dogs which survived the first rapid decline usually lived for at least three and one-half months. These facts should be noted by surgeons who are tempted to "drain off the poisons" in cases of clinical jaundice.

The appetite was moderate and but little difficulty was encountered in making the dogs eat. Changes in diet, however, were not well tolerated, and often implied a period of starvation. The loss of weight brought about a certain lethargy in some cases, but most dogs remained playful and very active almost into the terminal stages. Some appeared unduly excitable and boisterous when taken from the cages for their daily exercise. We came to regard any lethargy or depression as an indication that something was wrong with the fistula. One dog gave birth to a litter of pups on the twenty-seventh day after operation and lived nearly four months longer. Death usually occurred without any characteristic findings and was apparently due simply to inanition and rapidly oncoming weakness. The diet was varied only slightly and was in general well tolerated, although it was impossible to avoid attacks of diarrhea. These attacks did not seem to be related to any changes in diet but could be fairly regularly induced by the addition of fat to the diet. On the other hand, a huge addition of fat might not cause any disturbance at all. The same condition in patients with biliary fistula was previously reported on by Andrews, Hrdina and Dostal<sup>29</sup>. It is

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<sup>29</sup> Andrews, E., Hrdina, L., and Dostal, L. E. Etiology of Gallstones. II. Analysis of Duct Bile from Diseased Livers, *Arch Surg* 25: 1081 (Dec.) 1932.

maized the literature and discussed the relation of the condition to osteomalacia

According to most of the early chemists, bile was either neutral or slightly alkaline to litmus (Hammarsten). When more accurate studies became possible, it was revealed how slight was this alkalinity. Previous studies on the  $p_H$  of liver bile have given rather a wide range of values. Okada<sup>43</sup> found that in the dog it ranged a trifle over 8. Duttman's figures, both for dogs and human beings, showed it a trifle lower. In the prolonged and detailed studies of Drury, McMaster and Rous, the usual finding was about  $p_H$  8.2, although on standing the alkalinity might increase considerably. Neilson and Meyer<sup>44</sup> found the  $p_H$  of fresh bile from the liver to lie within this same range but emphasized the point that on standing it might go up to 8.4 or 8.6 and attributed this to loss of carbon dioxide. Drury emphasized the point that bile is a very well buffered solution and that addition of a considerable amount of acid is necessary to change its reactions appreciably. The recent investigations of Jones<sup>45</sup> called attention to the considerable buffer action of the large amount of sodium bicarbonate present, and he stated that this approximates that in pancreatic juice, which has long been known to contain so much that it froths violently on addition of strong acid.

Our studies have indicated that the  $p_H$  of bile, both that from the dog and that from the human being, is considerably lower if the bile is taken absolutely fresh<sup>46</sup>. It has generally run between 6.18 and 7. There seems to be a great lack of equilibrium, as the carbon dioxide concentration of fresh bile from the liver is usually over 100 in a series of nearly a hundred estimations in dogs. This carbon dioxide concentration at such a  $p_H$  gives of course a decidedly supersaturated solution, and great care must be taken in its collection to prevent its giving off large amounts of carbon dioxide. This occurs when the bile stands in the gallbladder, for then its carbon dioxide content is about one third as much in spite of considerable concentration.

Ross<sup>45</sup> found from 430 to 460 mg per hundred cubic centimeters of chlorides in human bile drained from a fistula, and Wangensteen<sup>1</sup> was able to get about 0.4 Gm of sodium chloride a day in bile from one of his patients. Bile obtained from a fistula, according to our experience

43 Okada, S. On the Secretion of Bile, *J. Physiol.* **59** 457, 1915

44 Neilson, N. M., and Meyer, K. F. Reaction and Physiology of Hepatic Duct and Cystic Bile of Various Laboratory Animals, *J. Infect. Dis.* **28** 510, 1921

45 Jones, K. K. Comparison of Buffer Value of Bile and Pancreatic Juice Secreted Simultaneously, *Proc. Soc. Exper. Biol. & Med.* **28** 567, 1931

46 Aronsohn, H. G., and Andrews, E. Nonbacterial Cholecystitis: Mechanism of Acidification of Bile in the Gallbladder, *Proc. Soc. Exper. Biol. & Med.* **33** 89, 1935

and Whipple<sup>35</sup> said, "a complete dissociation of the constituents of the bile" In a previous report<sup>24</sup> it was shown that in the case of the human being the bile collected in the morning was considerably less than that obtained in the afternoon or at night These results agree with the findings of Whipple and of Ross In the present experiments the amount collected during the day was inclined to be considerably larger than that at night, although the differences were not nearly so pronounced as in the human being

A brief summary of the various theories of the causes of acholic cachexia is necessary in orienting oneself, but these theories will be discussed in detail along with the portions of our work having a bearing on them

- 1 Anemia due to loss of pigment from the body
- 2 Anemia due to inability to absorb vitamin D
- 3 Acidosis due to loss of unbalanced ions in the bile
- 4 Hemorrhages from gastric or duodenal ulcers produced by the lack of alkaline bile in the duodenum
- 5 Fat starvation from inability to absorb fats in the absence of bile from the intestine
- 6 Avitaminosis from inability to absorb vitamin D With this must be considered the factor of anemia as well as the often reported factor of osteoporosis
- 7 Disturbance in the calcium metabolism due either to loss in the bile or to inability to absorb calcium from the acholic intestine The hemorrhagic disturbances often reported in the later stages have been associated with this possibility
- 8 Lack of sterols in the body due either to loss in the bile or to inability to absorb them from the acholic intestine
- 9 Loss of the bile acids

#### ANEMIA DUE TO LOSS OF PIGMENT FROM THE BODY

In a considerable portion of the literature on acholic cachexia, it is said that an invariable accompaniment is the development of profound anemia, and many observers believe that this is a cardinal factor in the picture Balfour and Ross,<sup>7</sup> Wangenstein,<sup>1</sup> Balderston,<sup>36</sup> Ross,<sup>15</sup> Pfaff

35 Wisner, F. P., and Whipple, G. H. Bile Salt Metabolism Variations in the Output of Bile Salts Pigments During Twenty-Four Hour Periods, *Am J Physiol* **60** 119, 1922

36 Balderston, S. V. Anemia Associated with Biliary Fistula, *Arch Int Med* **50** 223 (Aug) 1932

as chlorine <sup>49</sup>) before operation was 290 mg per hundred cubic centimeters, and at the conclusion of the experiment was 293 mg per hundred cubic centimeters, a change quite within the limits of experimental error. These animals were all on mixed diets containing much meat, and the onset of the cachexia was prompt and typical.

It seems justified, therefore, to assume that if the typical picture of cachexia cholipriva may be produced without changes in the acid-base equilibrium this factor is not fundamental, and that when reported by others it must be assigned to some intercurrent or indirect cause and must not be considered as a fundamental etiologic factor. While acidosis, as reported by many, may be a frequent accompaniment of acholic cachexia and may explain some of its manifestations, it seems wisest to attribute it to infection of the fistulous tract rather than to loss of bile.

#### PEPTIC ULCER

To all students of biliary physiology the duodenal ulcer has been the cause of many disappointments. It is an old and familiar story that just about the time that an experiment reached the critical stage, after much time and energy had been expended, sudden death occurred because of massive hemorrhage from the ulcerated stomach or duodenum. This danger is ever present in all experiments in which there is an absence of bile from the duodenum, whether produced by fistula or by obstruction of the common duct. The onset of these ulcers is usually prompt, generally occurring in the second week <sup>50</sup>. The ulcers are usually in the duodenum but not seldom in the pyloric portion of the stomach. They vary all the way from minute erosions to large callous ulcers typical of those observed in the clinic. Perforation of the deeper type is not uncommon, and hemorrhage is distressingly frequent. In the hands of most surgeons the administration of alkali has been of little value, although Kim and Ivy <sup>50</sup> reported that 1 Gm of gastric mucin a day will prevent duodenal ulcer.

In our own experience, in animals with either jaundice or biliary fistula such ulcers have been distressingly frequent, although no records are available as to the percentage of their incidence. Bollman and Mann <sup>51</sup> in an extensive study found that they occurred in 60 per cent of the cases of ligation of the common duct. Kapsinow, Engle and Harvey <sup>19</sup> found seventeen in forty-three dogs on which cholecystneph-

49 Whitehorn, J. C. Simplified Method for the Determination of Chlorides in Blood or Plasma, *J Biol Chem* **55** 499, 1921.

50 Kim, M. S., and Ivy, A. C. Prevention of Experimental Duodenal Ulcer by Feeding Neutral Gastric Mucin, *J A M A* **97** 1511 (Nov 21) 1931.

51 Bollman, I., and Mann, F. C. Peptic Ulcer in Experimental Obstructive Jaundice, *Arch Surg* **24** 126 (Jan) 1932.

In order to evaluate the possibility that loss of pigment is a factor in producing anemia one must review the salient points in the formation of pigment. Hemoglobin is the starting point and the question is at just what step in its degradation its usefulness to the organism ceases. The first stage is the separation of the huge globin molecule. The residual hematin is a non-bearing pigment closely related to bilirubin, which undoubtedly takes its origin from it by the removal of the single iron atom. An intermediate stage may be the highly toxic hematoporphyrin (said to be an isomere of bilirubin), which is thought by some to cause the toxic symptoms of jaundice, as it produces intense itching if injected into animals. Bilirubin is converted into biliverdin and then into urobilin and stercobilin, the possibly identical pigments found respectively in the urine and stools. Most students deny that there is any absorption or further utilization of the bile pigments from the intestinal tract. This is in direct opposition to the position of the bile acids as the enterohepatic circulation of these, as shown by Whipple and his associates<sup>39</sup> is an important feature in body economy. If hemoglobin is fed to an animal with a biliary fistula there is a definite rise in the pigment content of the bile, but if bile pigments are fed this rise does not take place—direct evidence of their nonabsorption.<sup>40</sup> It appears, therefore, that after the blood pigments have lost their iron they are no longer capable of reconstitution into carriers of oxygen and hence represent a waste product. On theoretical grounds therefore one cannot expect that the interruption of any such process by the production of external biliary fistula will bring about any deficiency in hematogenesis.

Our results agree with none of those previously reported by other authorities except Whipple and his associates. In other words in the animals which were carefully cared for anemia of any degree simply did not occur. However in some previous experiments in which we used preparations other than the Dragstedt cannula massive hemorrhage from gastro-intestinal ulceration often produced profound anemia and in other previous experiments severe anemia, obviously based on sepsis, was common.

Tables 1 to 4 show the blood picture of four dogs which survived for from four and one-half to five and one-half months with complete biliary diversion and died with the typical symptoms of cachexia cholipriva. Frequent blood counts and estimations of hemoglobin showed that the anemia was of trifling degree and did not approach in severity

39 Foster, F. M., Hooper, C. W. and Whipple, G. H. Metabolism of Bile Acid. IV. Endogenous and Exogenous Factors. I. *Biol. Chem.* **38**: 393, 1919.

40 Whipple, G. H. Origin and Significance of the Constituents of Bile, *Physiol. Rev.* **2**: 440, 1922.

even in the total absence of bile Jones<sup>45</sup> found that the buffering power of the pancreatic juice considerably exceeded that of the bile, and that the two seemed to act in a compensatory manner. When that of the bile fell, that of the pancreatic juice rose, and vice versa.

If it is possible, then, to carry dogs as a routine through the whole course of acholic cachexia without the formation of ulcers by any method, it seems reasonable to attribute the well known tendency toward ulceration to some concomitant feature and not to lack of alkali alone. While obviously this must be an important feature, it just as obviously cannot be the sole one. Possibly the suggestion of Still and Carlson<sup>44</sup> is relevant. They showed that damage to the liver had a potent effect on the motility of the stomach, and it is quite conceivable that as damage to the liver was minimal in our dogs its absence may help to account for lack of peptic ulcers. Heller<sup>55</sup> and many others have reported a hemorrhagic diathesis in the presence of a complete biliary fistula. This may be cured by the addition of bile to the diet. Some have considered this as a manifestation of damage to the liver and others as due to a lack of calcium and to be related to the osteoporosis. However, such a condition is often suggested by the gross appearance of the ulcers seen in biliary diversion, as multiple minute punctate submucous hemorrhages are a common finding.

#### FAT STARVATION

On the authority of Claude Bernard we assumed that the digestion of fat is totally abolished in the absence of bile from the intestinal tract, and in spite of the obvious fact that his experiments did not justify such a sweeping conclusion one constantly encounters the same statement today. Pflüger,<sup>56</sup> Dastre<sup>57</sup> and later Levin<sup>58</sup> arrived at a similar conclusion, using the same general criterion, i. e., absence of milky chyle in the lymphatic vessels draining the acholic portion of the intestine. The conclusion is backed also by the well known clinical occurrence of fatty stools in the case of jaundice and of biliary fistula, as well as by the intolerance of fats and the frequent attacks of diarrhea due to the presence of fatty acids. While most workers have felt that the

54 Still, K. S., and Carlson, A. J. Motor and Secretory Activity of Stomach During Acute and Chronic Obstructive Jaundice in Dogs, *Am J Physiol* **74** 34, 1929.

55 Heller, E. Hamorrhagische Diathese ohne Ikterus bei vollständiger ausser Gallenfistel, *Deutsche Ztschr f Chir* **235** 667, 1932.

56 Pflüger, E. Die Resorption der Fette vollzieht sich durch, dass sie in wässrige Lösung gebracht werden, *Arch f d ges Physiol* **86** 1, 1901.

57 Dastre, A. Du rôle de la bile dans la digestion des matières grasses, *Compt rend Soc de biol* **4** 782, 1887.

58 Levin, I. Ueber den Einfluss der Galle und des Pankreassaftes auf die Fettresorption im Dünndarm, *Arch f d ges Physiol* **63** 171, 1896.

that even in complete biliary deprivation anemia does not necessarily occur, and when it does it must be attributed to some complication, not necessarily to the direct deprivation of bile

### ACIDOSIS

Acidosis due to the loss of alkaline bile has been considered a factor in biliary cachexia by many observers. Since the time of Pavlov<sup>41</sup> this has been associated with the bony changes and other features of the

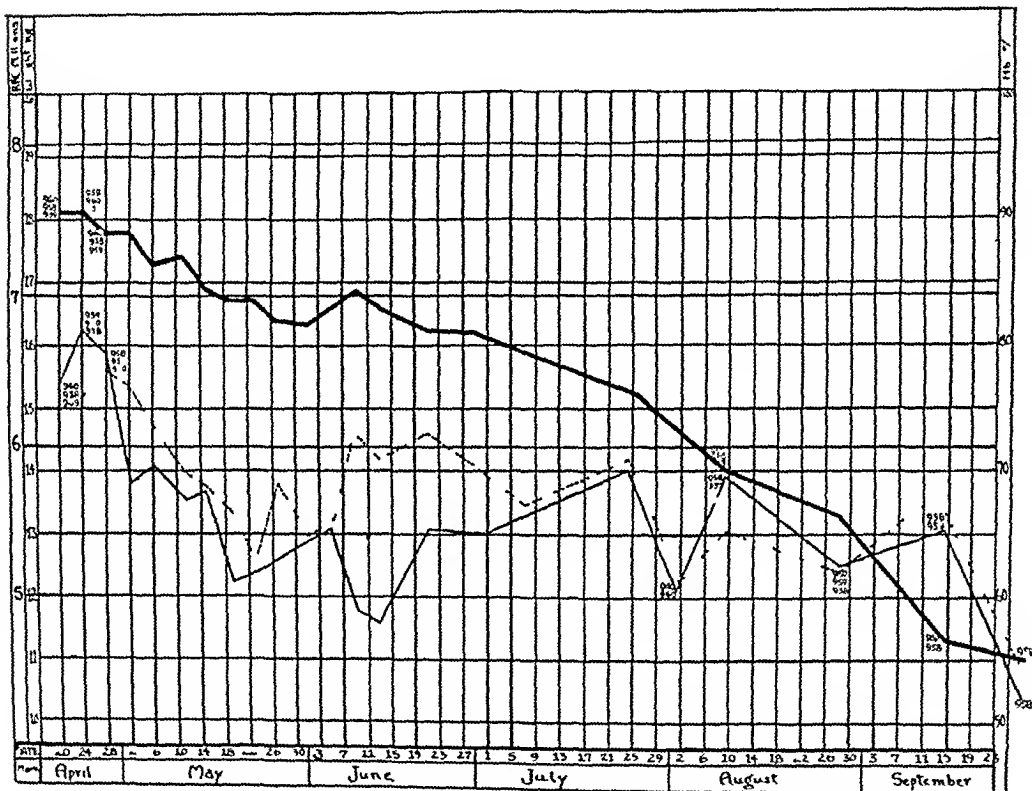


Fig 2—Average values on four dogs, showing the relation of anemia to icholic cachexia. The heavy solid line indicates the weight, the light solid line the red blood cell count, and the dotted line the hemoglobin content. Note the early initial slight drop and the maintenance of the level of the red cell count and the hemoglobin content until just before death. The loss of body weight was far more rapid and progressive.

disease. Balfour, Ross, Wangenstein and many other observers noted acidosis in clinical and experimental cases. Duttman, in 1927,<sup>42</sup> sum-

41 Pavlov, I. P. *The Work of the Digestive Glands*, translated into English by W. H. Thompson, ed. 2, London, C. Griffin and Company, 1910.

42 Duttman, G. *Die Veränderung des Saure-Basengleichgewichtes nach Gallen fisteln und ihre Bedeutung bei der Entstehung der sogenannten porotischen Mahreie*, Beitr. z. klin. Chir. **139** 720, 1927.



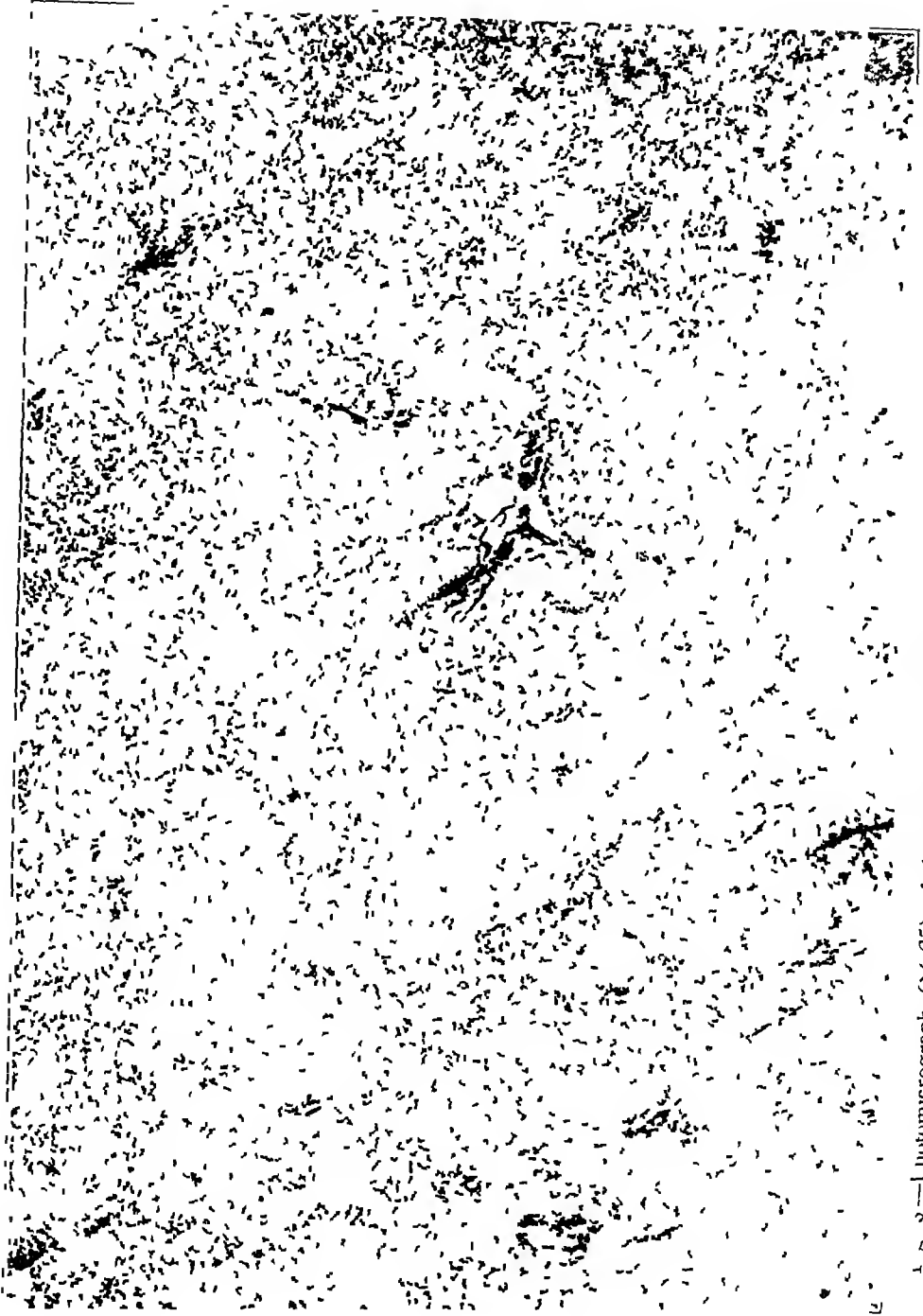


Fig. 3.—Photomicrograph ( $\times 25$ ) of the liver from a dog that survived ligation of the common duct sixteen months. Note the almost complete replacement of the parenchyma with fat.

as well as that of others, contains about the same amount of chlorides as serum does, and therefore theoretically one might expect that the loss of chloride would more or less parallel the theoretical loss of chloride in a hemorrhage of equal amount. This certainly represents an upper limit of possible loss of chloride. It is quite clear, then, that the total possible loss of chloride falls far within the range that may be and is easily made up in the food. No comparison is possible with the extensive, rapidly fatal loss of chlorides in gastric fistula.<sup>47</sup>

No free base is found in bile, and all the sodium not present as carbonates or chlorides is bound to bile acids. The other electrolytes

TABLE 6—Data Showing the Acid-Base Equilibrium in Eight Dogs Studied for Periods of from Twelve to Eighty Days After Operation

Days after Operation	Cholecystostomy 640		Cholecystostomy 639		Cholecyst nephrostomy 745		Cholecyst nephrostomy 678		Dragstedt Cannula 824		Cholecyst nephrostomy 680		Cholecyst nephrostomy 699	
	CO <sub>2</sub>	Cl	CO <sub>2</sub>	Cl	CO <sub>2</sub>	Cl	CO <sub>2</sub>	Cl	CO <sub>2</sub>	Cl	CO <sub>2</sub>	Cl	CO <sub>2</sub>	Cl
(Normal values before operation)	%		%		%		%		%		%		%	
4	42	294	40	300	36	294	32	288	36		41	305	40	294
8	42	296	42	294	29	299	40	306	33		48	274	39	277
12	40	297	40	272	26	299	34	294	35		27	311	43	250
16	42	307	38	327	23	305	42	289	29		29			
20	37	299	37	283	29	299	32	310	25		28	283		
24	33		31	349	32	310	27	307	36		33	316		
28	35	305	35	305	25		32	316						
32	27	305	30	371	30		30	316						
36	33	316	40	427	29		39	332						
40	46	310	46	305	21		33	321						
44	31	348	35	288	25		35	305						
48	31	310	34	327	41									
52	31	327	33	337										
56	36	357	42	300										
60	39	305	24	294										
64	42	310	34	310										
68	40		32											
72	37		42											
76	32		36											
80	36													
	30													

are present in quantities too small to consider in relation to the normal dietary intake. Therefore there seems to be no theoretical reason to expect changes in the acid-base equilibrium as a direct result of loss of either anions or cations in the bile (table 6).

This has been exactly our experience. Eight dogs were studied for periods ranging from twelve to eighty days after operation, and the results are tabulated in table 6. The average carbon dioxide-combining power, according to Van Slyke and Cullen,<sup>48</sup> at the conclusion of the experiment was exactly the same as in the control estimations before the experiments began (39.5). The average chloride content (expressed

<sup>47</sup> Dragstedt L. R., and Ellis J. C. Fatal Effect of Total Loss of Gastric Juice, *Proc Soc Exper Biol & Med* 26 305, 1929.

<sup>48</sup> Van Slyke, D. D. and Cullen G. E. Studies on Acidosis, *J Biol Chem* 30 289 1917.

Thus while it is undoubtedly true that absorption of fat is markedly diminished in acholic cachexia, it is clear that moderate amounts are absorbed and that actual fat starvation does not take place

#### AVITAMINOSIS

As a corollary to the theory that there is a lack of fat absorption goes the concept that fat-soluble vitamin, a sterol, is not absorbed from the intestine in the absence of bile. This attractive hypothesis is also closely related to the factor of anemia and to the frequently reported disturbances in calcium metabolism and associated osseous changes. Furthermore, a tremendous amount of evidence for this theory has been built up on the basis of careful experimental studies. The factor of anemia has been discussed, and the disturbances in calcium metabolism will be considered separately.

The effects of viosterol on various manifestations in an animal with a biliary fistula have been studied by many observers, and a definite correlation has been reported almost unanimously. The apparently overwhelming nature of the evidence presented, together with the utterly negative results of our experiments, warrants a review of the subject. Seifert,<sup>63</sup> Seyderhelm and Tammann,<sup>64</sup> Emerson,<sup>65</sup> Murakami,<sup>66</sup> Heymann,<sup>67</sup> Greaves and Schmidt,<sup>68</sup> Dietrich,<sup>69</sup> Heller,<sup>65</sup> Seyderhelm and Tammann,<sup>37a</sup> Baumann,<sup>37b</sup> Takasu<sup>70</sup> and Whipple and his associates<sup>36b</sup> reported experiments indicating a direct relationship of acholic cachexia to lack of fat-soluble vitamin. Evidence of various sorts was included. Tammann<sup>64b</sup> found that the osteomalacia associated with acholic cachexia could be prevented and cured by injection of activated ergosterol. Later,

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63 Seifert, E. Zur Frage der porotischen Malazie nach Gallen fisteln, Beitr z klin Chir **136** 496, 1926

64 (a) Seyderhelm and Tammann<sup>37a</sup> (b) Tammann, H. Ueber die Beeinflussung der porotischen Osteomalazie nach Gallen fistel durch das D-Vitamin, Beitr z klin Chir **142** 83, 1928

65 Emerson, W. C. Distribution of Calcium in Jaundiced and Acholic Dogs, J Lab & Clin Med **14** 122, 1928

66 Murakami, K. Ueber die Gallensaurebildung, Avitaminosen und Gallensaureausscheidung in der Galle, J Biochem **9** 321, 1928

67 Heymann, W. Untersuchungen über die Phosphatstoffwechselstörung bei Rachitis, über Rachitis und Tetanie bei Gallen fistelhunden, Ztschr f Kinderh **54** 201, 1933

68 (a) Greaves, J. D., and Schmidt, C. L. A. Studies on Calcium and Phosphorus in Bile Fistula Dogs, Proc Soc Exper Biol & Med **29** 373, 1932, (b) The Role Played by Bile in the Absorption of Vitamin D in the Rat, J Biol Chem **102** 101, 1933

69 Dietrich, H. Die porotische Malacie nach Gallen fistel, Beitr z klin Chir **134** 530, 1925

70 Takasu, M. Experimentelle Studien über die acholische Kachexie, Deutsche Ztschr f Chir **224** 240, 1930

rostomy had been performed Kim and Ivy found ulcers in 10 per cent of dogs in which the common duct had been tied and in 60 per cent of those in which the Rous fistula was used Berg and Jobling,<sup>52</sup> using a Rous fistula, found peptic ulcers in thirteen of twenty-three dogs These figures represent a considerably higher incidence than our experience indicates but are in accord with the fact that the Rous type of fistula with the cannulation of the common duct close to the duodenum is especially provocative of ulcer Kim and Ivy suggested that the mechanical irritation of the tubing in this neighborhood is a factor This observation is interesting in view of the finding of Elman and Hartmann<sup>17</sup> that a fistula alone causes ulcers in but few cases In our own hands the Rous fistula was conspicuously unsuccessful technically and, as stated previously, caused many ulcers Elman as well as Rous, had considerable technical success and reported few ulcers

Berg and Jobling<sup>52</sup> suggested that the general condition of the dog and the hygienic conditions under which it is kept are important factors He found that ulcers developed in 100 per cent of dogs under ordinary management, but that by providing special care of a general type this percentage was reduced to 30 He was able to construct smoothly functioning Rous fistulas, and but few ulcers occurred

Our experience in the use of the Dragstedt cannula proved quite surprising, to us at least Instead of losing a high percentage of animals because of the development of ulcers, we did not lose a single one of over thirty dogs Careful postmortem examination and constant examination of the stools for blood (chemical as well as gross) gave negative results in all cases In not a single dog did either gastric or duodenal ulceration occur

The explanation of this phenomenon is difficult The cachexia was usually of a very advanced grade, and most of the animals that lived long lost over one third of their body weight Certainly their "general condition," in the sense discussed by the aforementioned authors, was the worst possible It appears necessary to reconsider our former hasty conclusion that lack of alkaline bile is the sole factor In the first place the alkalinity of bile is minimum although considerable buffering power is present, as was discussed before McRoberts<sup>53</sup> studied the  $p_H$  of the duodenal contents following exclusion of bile and found that it was changed only to a minimum degree In fact the change was so negligible that he concluded that the buffering action of the pancreatic juice was sufficient to prevent any acidity of the duodenal contents

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<sup>52</sup> Berg, B. N., and Jobling, J. W. Biliary and Hepatic Factors in Peptic Ulcers. An Experimental Study, *Arch Surg* 20 997 (June) 1930

<sup>53</sup> McRoberts, J. W. Effect of Exclusion of Bile on Reaction of Duodenal Contents, *Proc Staff Meet, Mayo Clin* 7 453, 1932

The loss of body weight proceeded at the same general rate as in control animals, and life was not prolonged

One curious feature may be worth noting, that is, the profound dependent terminal edema that occurred in four dogs of the series to which viosterol was administered. The edema was marked in all four paws and the anterior abdominal wall. In view of the fact that edema in a dog is an unusual occurrence and is produced experimentally only with considerable difficulty, two of these animals were studied by Dr L. Leiter, who contributed the following data. The blood proteins

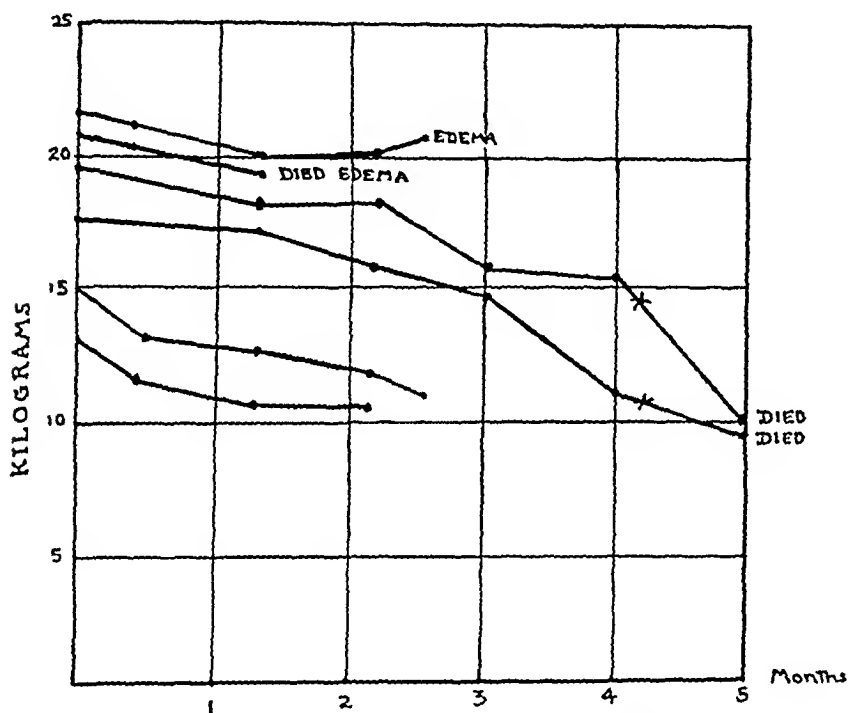


Fig 4—Chart of the body weights of six dogs with biliary fistula, to which viosterol was given hypodermically. The dogs with the two longest weight curves were given viosterol only after the point on the curve marked X. Others received it from the beginning of the experiment. Loss of weight occurred at the same rate in the experimental animals as in the controls (fig 2).

were only moderately lowered, being just about at the lower threshold of normal. The kidneys were normal at autopsy, both grossly and histologically. We have no explanation to offer for this phenomenon, and none of our animals except those treated with viosterol became edematous.

One dog, on the seventeenth postoperative day, had a single tetanic convulsion lasting about fifteen minutes. At this time the blood calcium was 12.4, the highest found at any time in his course, at the same time

digestion of proteins and carbohydrates was normal or nearly so in the absence of bile, it is quite clear that the emulsification and absorption of fat are seriously retarded. Rachford<sup>59</sup> showed that the action of pancreatic lipases was increased threefold by the addition of bile and that the constituents of the bile which had this function were the bile salts. He was able to produce in vitro the digestive powers of bile quantitatively with pure bile salts. Von Furth and Schutz<sup>60</sup> showed that bile, added to pancreatic secretions in about the proportion found in the intestine, increased their fat-splitting powers ten times.

In spite of all this evidence, there is just as clear proof that the power to utilize fats in the absence of bile from the intestine is not totally lost. In the first place, animals dying from jaundice or a complete biliary fistula do not lose all their fats and in the former case may live for more than a year. If absence of bile causing fat starvation is the important factor in such cachexia, it is difficult to explain why jaundice is so well tolerated and the fistula is not. Furthermore direct evidence is not lacking. While alimentary lipemia of a high degree cannot be produced in animals with fistulas, a slight postprandial rise can be seen. Umber was unable to recover more than about one half of the ingested fat from the stools, and bacterial action sufficient to account for such a destruction seems most unlikely. Munk's<sup>61</sup> elaborate studies of the question indicate that in favorable circumstances as much as one half of the fat may be absorbed and that usually from 10 to 20 per cent can be accounted for in no other manner except by assuming its absorption and utilization.

On the other hand, there is considerable recent literature indicating that direct absorption of fats into the blood stream is possible. The method recently demonstrated by Verzar and Kúthy,<sup>62</sup> however, requires the presence of bile in the intestine, and it seems more rational to assume that absorption of fat from the acholic intestine in diminished amounts must take place through the lacteals (fig. 3).

Our studies justify the general conclusions of the last authors on several grounds. 1. Postmortem examination fails to show a specific

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59 Rachford, B. K. The Influence of Bile on the Fat Splitting Properties of Pancreatic Juice, *J. Physiol.* **12** 72, 1891.

60 von Furth, O., and Schutz, J. Ein Beitrag zur Methodik der Versuche über Fettresorption aus isolierten Darmschlingen, *Beitr. z. chem. Phys. u. Path.* **10** 462, 1907.

61 Munk, I. Ueber die Resorption von Fetten und festen Fettsäuren nach Ausschluss der Gallen vom Darmkanal, *Virchows Arch. f. path. Anat.* **122** 302, 1890.

62 Verzar, F., and Kúthy, A. Die Verbindung der gepaarten Gallensäuren mit Fettsäuren und ihre Bedeutung für die Fettresorption, Löslichkeit und Diffusibilität, *Biochem. Ztschr.* **210** 265, 1929.

matory conditions rapid absorption may occur<sup>74</sup> and in prolonged obstruction excretion is known to occur from the mucosa,<sup>75</sup> it seems safe to assume that in the normally functioning viscus no change in calcium content occurs except that incident to the concentration of the bile. If the usual volume of bile is from 10 to 20 cc per kilogram of body weight, it is easily calculated that the average dog might lose from 100 to 300 mg of calcium per day in drainage through a biliary fistula. If absorption is normal, this amount seems insignificant compared with the intake.

While Gilbert<sup>72</sup> found that the amount of calcium in the bile was about two thirds of that in the urine and that this secretion of calcium was not dependent on that in the urine, the large amount found in isolated segments of the intestine suggests that the major organ for the excretion of calcium is the intestine and not the kidney. Fecal calcium is usually far in excess of that in the urine. Thus in order to assume that disturbances in calcium metabolism are due to inability to absorb calcium directly it is first necessary to get concrete proof that such inability exists, and such proof is utterly lacking. Von Beznak<sup>76</sup> offered some evidence on this score. He showed that in dogs distinct alimentary calcemia was produced. Furthermore passage of this blood through the liver did not change its calcium content. In normal dogs the content of the portal blood is the same as that of the blood in the general circulation, but after biliary diversion it was less. These experiments seem conclusive, but the changes reported might be considered as lying within the limits of experimental error.

On the other hand, Brougher<sup>77</sup> noted that the development of parathyroid tetany was much delayed by ligation of the common duct and assumed that this might be explained by an actual increase in the absorption from the intestine. Heymann<sup>67</sup> made biliary fistulas in puppies, which normally produce a condition very like rickets. He found that this condition was alleviated by irradiated ergosterol but not by calcium, and it seemed logical to assume that therefore the simple absence of bile from the intestine did not interfere with the absorption of the

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74 Andrews, E., and Hrdina, L. Absorption of Calcium from the Gallbladder, *Am J M Sc* **181** 478, 1931

75 Phemister, D. B., Day, L., and Hastings, A. B. Calcium Carbonate Gallstones and Their Experimental Production, *Ann Surg* **94** 595, 1932

76 von Beznak, A. Der Einfluss der Galle auf die Resorption des Calciums, *Arch f d ges Physiol* **228** 604, 1931

77 Brougher, J. C. Effect of Ligation of the Common Bile Duct upon the Appearance of Tetany in Thyroparathyroidectomized Dogs, *Am J Physiol* **84** 39, 1928

loss of fats Much fat is found, and the distribution is normal Furthermore, the liver may often show an increase in fat 2 A slight alimentary lipemia is possible 3 The survival of certain jaundiced animals may be prolonged One, in particular lived for sixteen months and weighed more at death than before the operation The most striking aspect at autopsy was the extreme obesity and the extensive fatty infiltration of the liver The liver was nearly white and microscopic examination showed that nearly all the parenchymatous tissue had been replaced by fat (fig 3) Although measurement was impossible, there is no doubt but that this animal contained much more fat after sixteen months of absence of bile from the intestine Such a picture is certainly incompatible with the theory that in the absence of bile there is inability to absorb fats from the intestinal tract

We intended to study the fat balance in several of the dogs, but on account of the extreme difficulty in collecting the specimens this proved impossible In order to keep dogs in good health, periods of

TABLE 7—*Effect of Fifty Grams of Fat Administered Orally on the Fat Content of the Blood*

	Milligrams per Hundred Cubic Centimeters			
	77	83	107	127
Control	77	83	107	127
12 hours	115	88	125	133
18 hours	86	88	125	136
4 days	90	77	107	99

exercise outside the cages were necessary, and when the stools were liquid, as they often were many were lost or contaminated with material from the floors of the laboratory However, a series of seventy-nine estimations of blood fats were made on four dogs extending over their periods of cachexia (tables 1 to 4) These showed clearly that there was no lack of fat in the body as the values all fell within the normal limits Even dogs in the last stages of cachexia showed a fat content of the blood of about 0.1 per cent

Four dogs were submitted to tests for alimentary lipemia Fifty grams of fat was given by mouth In all four a rise occurred in the blood fats, and in two this was considerable The rise in one case was from 77 to 115 mg per hundred cubic centimeters While the rises were not comparable to those that occur in normal dogs they indicate that in the presence of a biliary fistula some fat is absorbed

Four other dogs with biliary fistulas were subjected to exploratory laparotomy and no whitish lacteals could be found but such changes in the blood fats as are seen in table 7 would probably not have altered the gross appearance of the lymph Nevertheless there is a possibility that the fat may be absorbed directly into the blood stream



(sixteen months) As can be seen, there is not the slightest sign of lacunar absorption, nor is there any thinning of the cortex of either bone. Roentgen studies in other cases have failed to show evidence of osteoporosis.

If it is possible to carry dogs through the entire course of typical cachexia cholipriva without osseous changes, one feels entitled to assume that these do not represent integral parts of the picture but are due to complications. In most of the previously reported cases both in human subjects and in animals the fistulas have been incomplete, as indicated by the long survivals. It may therefore be that osteoporosis in such cases is simply a manifestation of general cachexia and part and parcel of the widespread degenerative changes in all the organs. Many of the animals have been caged and many of the human subjects bedridden, and ordinary atrophy of the bones and muscles from disuse

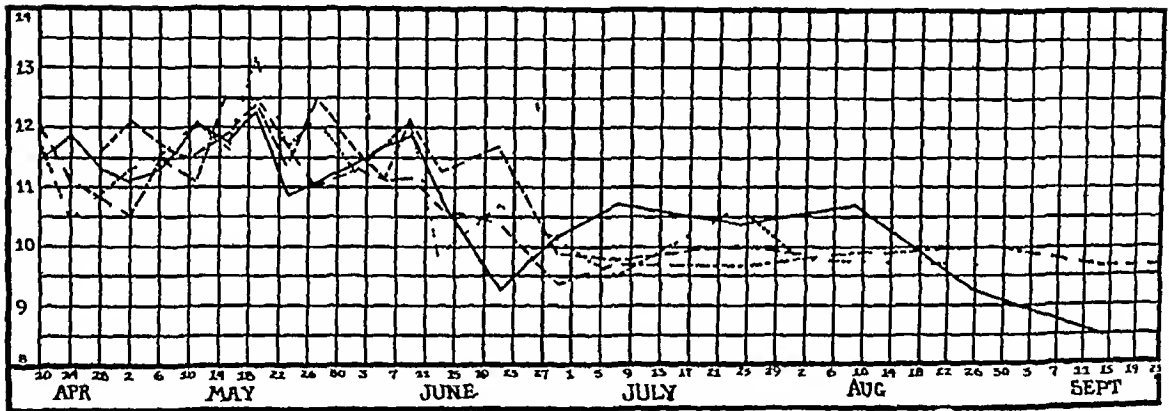


Fig 5—Chart showing the blood calcium curves of four dogs with acholic cachexia. Note the slight but definite lowering in all instances. The values are given in milligrams per hundred cubic centimeters. The broken line represents dog 940, the dot and dash line dog 958, the solid line dog 959, and the dotted line dog 960.

is possible. In any long continued severe disease osseous atrophy usually occurs, and parallels could easily be drawn in the clinic with such diseases as cancer, tuberculosis and pernicious anemia, in which prolonged invalidism or even old age has shown in roentgenograms conditions at least as typical as those often shown as being peculiar to biliary cachexia.

On the other hand, in the case of jaundice and of biliary fistula extreme osteoporosis may occur in the absence of bile from the intestine much too rapidly to permit these explanations. An alternative theory has been suggested by Duttman,<sup>42</sup> who attributed osteoporosis to acidosis. Although the changes in the acid-base equilibrium reported in his experiments would not ordinarily be considered severe enough

with Baumann,<sup>37b</sup> he showed that iron had little effect in acholic anemia. Liver extracts were of slight benefit. However, irradiation of the animals helped more, while irradiated bile was considerably more potent than normal bile. Heller<sup>50</sup> found that administration of vitamin D prevented the hemorrhagic changes. Murakami found that olive oil had no effect on the secretion of bile acids, while viosterol raised it fourfold. (Whipple had previously shown the same result.) Heymann<sup>67</sup> reported that osteomalacia occurring in puppies with biliary fistulas is curable by the administration of viosterol. The previously mentioned experiments of Greaves and Schmidt,<sup>68b</sup> indicating that a phosphorus-calcium balance was restored to osteoporotic animals by the administration of viosterol are pertinent to this subject.

It has been reported by some that the blood calcium of dogs with biliary fistulas may be raised by the subcutaneous injection of viosterol. That this is impossible has been not only our experience but that of all workers in the field of vitamins, for the blood calcium levels of normal dogs cannot be raised by this means. Three experiments of this type convinced us of the futility. The first experiment consisted of feeding a dog with a biliary fistula 20 cc of viosterol in oil 250 D. The effect on the blood calcium was nil. As controls two other normal dogs were each given the same dose, and the results were negative. This dose was said by a colleague who had used it previously to be about two thirds the lethal amount for a dog and that even the lethal amount would not cause a rise in blood calcium. It seems rational then to discard all experiments in which dogs have been used to test the effect of viosterol on the blood calcium unless there was a profound lowering of the calcium in the first place. It is well known that parathyroidectomized dogs respond to viosterol, but only if the blood calcium content is in the same range as that in the case of tetany.

There is also considerable literature on the osteoporosis caused by jaundice in which the same factors are acting. This condition was reviewed by Buchbinder and Kern,<sup>71</sup> who like Heymann<sup>67</sup> and others thought that it was rather typical rickets.

With this apparently overwhelming evidence at hand, it is difficult to explain our results. They were, briefly, that no benefit occurred from the administration of viosterol in apparently adequate doses. There was in our animals no anemia or osteoporosis to combat, and the only way of measuring the effect of the vitamin was to weigh the animals and to see if it prolonged life. As can be seen from figure 4 it had not the slightest effect.

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<sup>71</sup> Buchbinder, W. C., and Kern, R. Experimental Obstructive Jaundice. I. Growth Factor in Defective Calcification, *Arch. Int. Med.* **40**: 900 (Dec.) 1927. Blood Calcium Deficiency in Experimental Obstructive Jaundice, *Am. J. Physiol.* **80**: 273, 1927.

to cause loss of calcium, much wider fluctuations have been found by other observers. Calcium carbonate is more soluble in acid mediums. Hastings and his associates<sup>81</sup> presented tables and equations enabling one to predict its solubility at various concentrations of other electrolytes at various values of  $p_H$ . Bodansky, Jaffe and Chandler<sup>82</sup> showed that extreme decalcification may be produced by the administration of phosphorus, which does not necessarily raise the level of the blood calcium which is controlled largely by the renal threshold. Later they produced typical decalcification in animals by acidosis caused by other means and made it clear that a negative calcium balance results in any condition of prolonged acidosis. In view of the fact that an association of acidosis with acholic cachexia has been reported by many authors, this seems to offer a ready explanation of the decalcification which may accompany the cachexia. As we stated previously, we believe that acidosis results from infection of the fistula or from damage to the liver and that the absence of these features in our experiments may account for the absence of osseous changes so often said to be typical.

#### CHOLESTEROL

The question of the absorption of sterols from the acholic intestine is intimately related to the theory of lack of vitamin D. If it is true that bile salts are necessary to absorb lipoids as they have been said to be needed to absorb fats, it is clear that there should be a decided lack of sterols in the organism under such conditions. This has not proved true in our experiments. While it is well known that the blood cholesterol content in the dog averages considerably higher than in man, the normal fluctuations are very wide. The uncertainty and inaccuracy of the methods usually applied for its estimation are perhaps partly accountable for these apparent fluctuations. Accurate cholesterol estimations can be made by only one method, i. e., the gravimetric one of precipitation with digitonin and weighing. This is impossible in using specimens as small as samples of blood necessitate (or even samples of bile). Therefore one of the various modifications of the Autenrieth-Funk color reaction is used, and in our hands the percentage of error was at least 20 per cent. We were never able to attain the degree of accuracy recently reported by some observers, who claimed that they had reduced this percentage of error to less than 3. The

81 Hastings, A. B., Murray, C. D., and Sendary, J. Studies of the Solubility of Calcium Salts, *J. Biol. Chem.* **71** 731, 1931.

82 Bodansky, A., Jaffe, H. L., and Chandler, J. P. Serum Phosphatase Changes in Calcium Deficiency and in Ammonium Chloride Osteoporosis, *Proc. Soc. Exper. Biol. & Med.* **29** 871, 1932. Bodansky, A., and Jaffe, H. L. Phosphatase Studies. Serum Phosphatase of Non-Osseous Origin, Significance of Variations of Serum Phosphatase in Jaundice, *ibid.* **31** 107, 1933.

a corneal opacity developed, which was attributed to avitaminosis by an ophthalmologist. However, the opacity disappeared spontaneously within ten days, and the dog survived for three months longer. This incident shows how easily data on avitaminosis may be misinterpreted.

Four other animals treated with viosterol showed marked increase in weight and general well-being. The coats became glossy and the appetite increased. Each of these animals was found to have an accessory duct, or the old ones reestablished, and to have small amounts of bile in the stools, which of course was the cause of the recovery. Such accidents may explain some of the previously reported results but certainly not all of them in the hands of many careful workers. On the other hand it does not seem exactly logical to assume, as many workers have, that just because viosterol may cure some of the manifestations of acholic cachexia, lack of viosterol is the direct cause of it. According to such logic, if, for instance, malaria is cured by quinine, it must be caused by lack of quinine.<sup>1</sup> Whipple and his associates<sup>38b</sup> were careful not to reason thus, and although they reported that viosterol improved the blood picture in the cachectic dogs, they did not state that lack of it is the cause of the anemia. Viosterol is a powerful stimulant to osseous deposition, and the fact that it helps osteoporosis is not proof that lack of it causes the osteoporosis.

#### DISTURBED CALCIUM METABOLISM

Disturbances in calcium metabolism have been reported on by many authorities, some of whom considered it a direct result of avitaminosis, while others, beginning with Klinker, postulated inability to absorb calcium from the acholic intestine. The frequency with which osteoporosis has occurred in acholic cachexia is shown by the long series of papers on the subject.

Gilbert<sup>72</sup> first called attention to the possibility of serious loss of bile in cases of external drainage and spoke of this excretion as a specific function of the liver. On the other hand, many observers have found that the calcium of the bile from the liver usually fell within the range of that of the blood, although it is often slightly higher. In our laboratory in a series of sixteen dogs it averaged 13 mg. per hundred cubic centimeters. In the usual concentration in the gallbladder this paralleled the rise in the total solids for short periods such as fall within the time the bile ordinarily remains in the viscus.<sup>73</sup> Although in inflam-

<sup>72</sup> Gilbert, E. Ueber die Kalkausscheidung durch die Galle, *Ztschr. f. d. ges. exper. Med.* **53** 539, 1924.

<sup>73</sup> Andrews, E., Schoenheimer, R., and Hrdina, L. Etiology of Gallstones. I. Chemical Factors and the Role of the Gallbladder, *Arch. Surg.* **25** 796 (Oct.) 1932.

is low, usually averaging under 10 mg per hundred cubic centimeters. In a few of our specimens much higher concentrations were found. These were clearly due to partial obstruction of the tube, allowing the bile to lie for periods in the gallbladder and to undergo concentration. That this is the correct explanation is shown not only by the finding of such obstructions but by the fact that during these periods the total daily excretion of cholesterol in the bile did not increase.

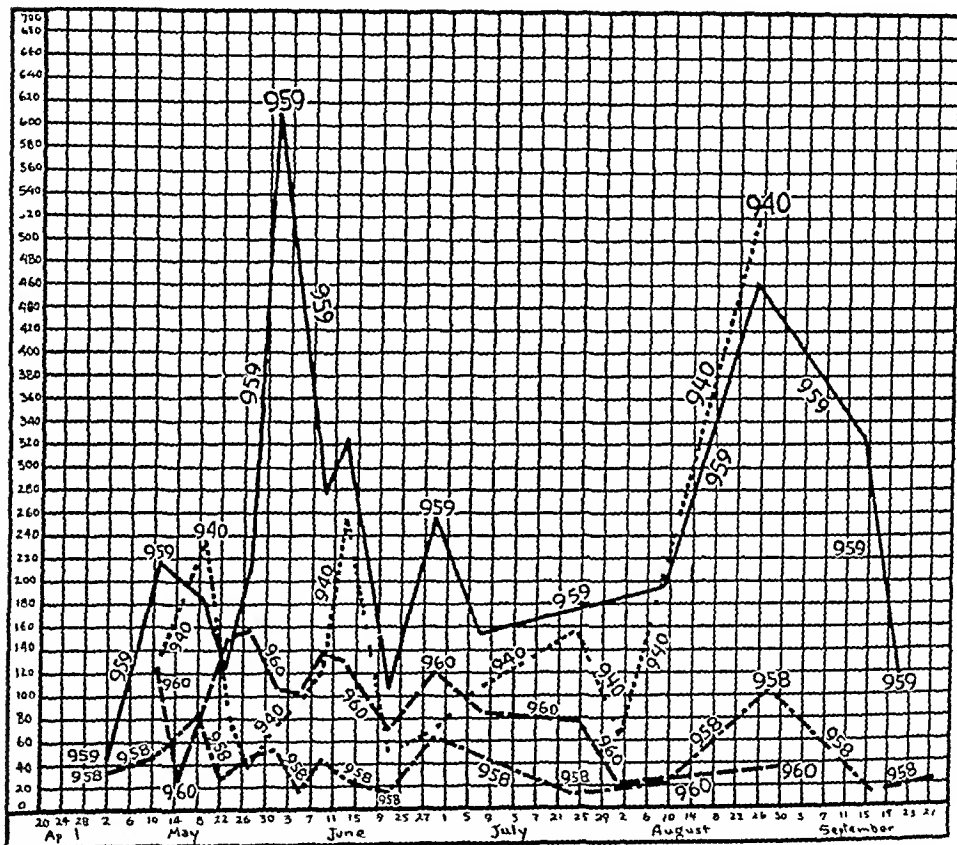


Fig 8—Graph showing the bile cholesterol curves of the dogs as given in tables 1 to 4. The dotted line represents dog 940, the dot and dash line dog 958, the solid line dog 959, and the dash line dog 960.

The evidence from these data is distinctly against cholesterol starvation. If it is then assumed that the cholesterol is exogenous (see comment under "The Sterol Balance"), one feels entitled to assume that it must be absorbed from the gastro-intestinal tract, and one is led to wonder why irradiated ergosterol should not be absorbed equally well, as it is decidedly more absorbable than ordinary sterols of animal origin.

calcium<sup>69</sup> Sekitoo<sup>78</sup> showed that there was a definite decrease in blood calcium in rabbits with biliary fistulas, and that this could be corrected by the administration of bile salts by mouth. Fuziwara<sup>79</sup> showed that the addition of bile to the diet causes a dog to excrete more calcium in the bile and less in the stools. Rose and Kohn stated the belief that in the absence of bile more calcium is absorbed and attributed this to the fact that much calcium may be bound in insoluble compounds with the bile acids in the normal person.

Many observers including ourselves, have found that the blood calcium and the blood phosphorus were normal in subjects with biliary fistulas. This is not exactly confirmed in our series of eighty estimations of blood calcium (tables 1 to 4). Although the figures toward the end are perhaps within the range of normal, it is quite clear that there is a decided change. In the period of preoperative control the average was about 12 mg per hundred cubic centimeters and it had as a rule dropped to about 9 mg in from four to five months. Neither figure by itself is significant, but if the entire series is plotted on a chart a fall is evident that is entirely beyond the limits of experimental error. Thus some disturbance in the calcium metabolism is evident. Thus decalcification of the skeleton, if it occurs, must be studied on the basis of the careful measurement of intake and output. This was done by Greaves and Schmidt, who demonstrated in rats and dogs that there was a negative phosphorus and calcium balance in the case of biliary fistula and that this returned to normal after the administration of viosterol and minute amounts of bile salts by mouth. Similar experiments on the human being by King, Bigelow and Pearce<sup>80</sup> gave similar results.

The evidence, while not complete, thus seems to point decidedly to a distinct disturbance of calcium metabolism in the case of biliary fistula. It is difficult to explain our results, which seem only to complicate the picture. These may be summed up in a word or two. In dogs with normally functioning biliary fistulas, in the absence of anemia, infection, periods of jaundice and other complications, osteoporosis did not occur. Two photomicrographs are shown, one representing the longest reported survival of a dog with a complete biliary fistula without accessory feeding (five and one-half months), and the other the longest reported survival of an adult dog with complete jaundice.

78 Sekitoo, T. Ueber den Einfluss der Gallensaure auf den Calciumstoffwechsel, *J Biochem* **12** 59, 1930, Beiträge zur Kenntnis der Glykcholsaure aus Kaninchengalle, *Ztschr f physiol Chem* **199** 225, 1931.

79 Fuziwara, K. Ueber den Einfluss der Gallensaure auf den Calciumstoffwechsel. Calciumausscheidung im Kot bei Zufuhr von Cholsaure, *J Biochem* **13** 465, 1931.

80 King, I. H. Bigelow, J. E., and Pearce, L. Experimental Obstructive Jaundice. *J Exper Med* **14** 159, 1911.

pointed out by Andrews, Schoenheimer and Hrdina in recent papers,<sup>7</sup> there is no proof that high blood cholesterol induces high bile cholesterol, and it has even been suggested by some that the mere fact that the blood cholesterol is high is indicative that the usual amounts are not excreted in the bile.<sup>86</sup> Others have shown that in the case of lipoid nephrosis in which the blood cholesterol is extremely high, the bile contains normal percentages. Pribram,<sup>87</sup> however, reported evidence that in the later stages of pregnancy and during the succeeding months the cholesterol in the bile is markedly increased. His studies were based on analyses of material aspirated from the duodenum, which one must realize is mixed with intestinal secretions which have a high sterol content, considerably higher in fact, than that of the bile.

With these points in view the findings on this animal are interesting (table 4). In the first place it is clear that there was no change in the blood cholesterol and that it lay in the same range as in the other three animals throughout the experiment. This is a distinctly different picture from that found in the human being, in whom the work of many observers shows that often there are at this period changes amounting to over 100 per cent. On the other hand, the changes in the bile were very striking. The average cholesterol content of the bile of the other three animals was 11 per cent, while that of the animal who went through the pregnancy was 25.7 per cent. The average amount excreted daily by the controls was 18.5 mg while the pregnant animal excreted 42.1 per cent daily. The total excretion of the controls averaged 1,359 mg while that of the pregnant animal was 4,229. These figures would be even more striking if the period studied included only the month before and the month after labor. It appears, therefore, that the cholesterol in the bile is increased at least threefold during the latter part of pregnancy and the month succeeding it.

In the dog the period of gestation is twelve weeks. Judging by the size and development of the fetuses they were about 8 weeks old, i. e., one month premature. The litter of seven weighed 1,960 Gm (not including amniotic fluid and placenta, which were lost). From these fetuses 3.46 Gm of cholesterol was extracted, a figure corresponding to about the normal percentage in blood. From table 4 it can be seen that the rise in bile cholesterol began at about the middle of the pregnancy and lasted for an equal period after delivery. Thus, applied to the human being, these figures should be multiplied by 3, the ratio of the two periods of gestation.

<sup>86</sup> Gainsborough, H. A Study of So-Called Lipoid Nephrosis, *Quart J Med* **23** 101, 1930. Fox, F. W. The Composition of Human Bile and Its Bearing upon Sterol Metabolism, *ibid* **21** 107, 1927.

<sup>87</sup> Pribram, E. C. Zur Frage des Cholesterinstoffwechsels während der Schwangerschaft und im Wochenbett, *Arch f Gynak* **120** 90, 1923.

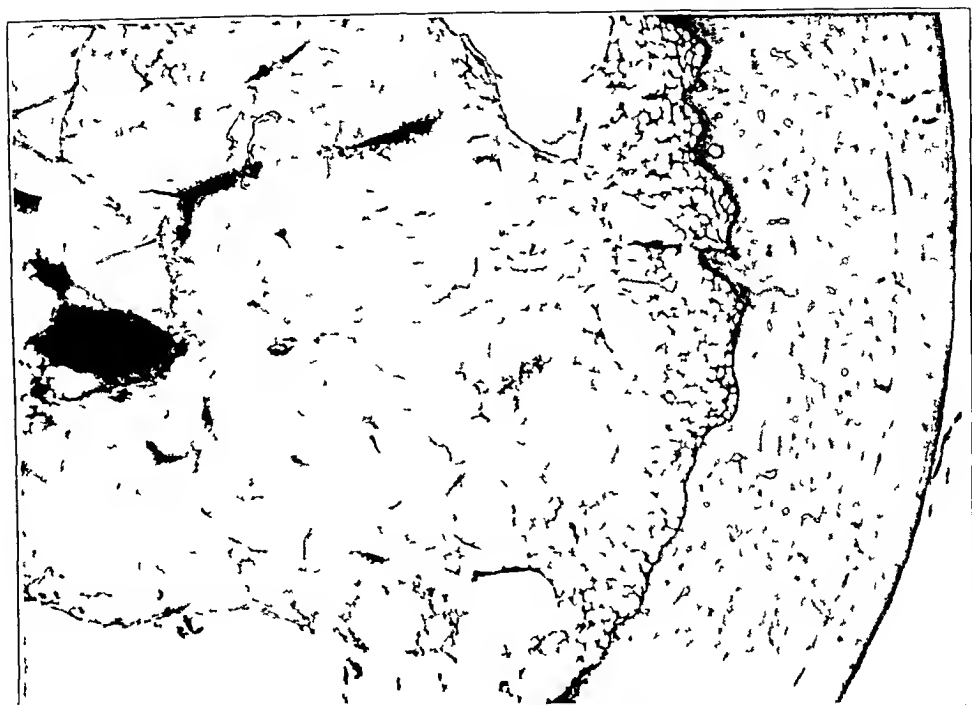


Fig 6—Photomicrograph ( $\times 18\frac{3}{4}$ ) of bone from a dog which survived fifteen months with complete biliary obstruction. Note the complete absence of osteoporosis.

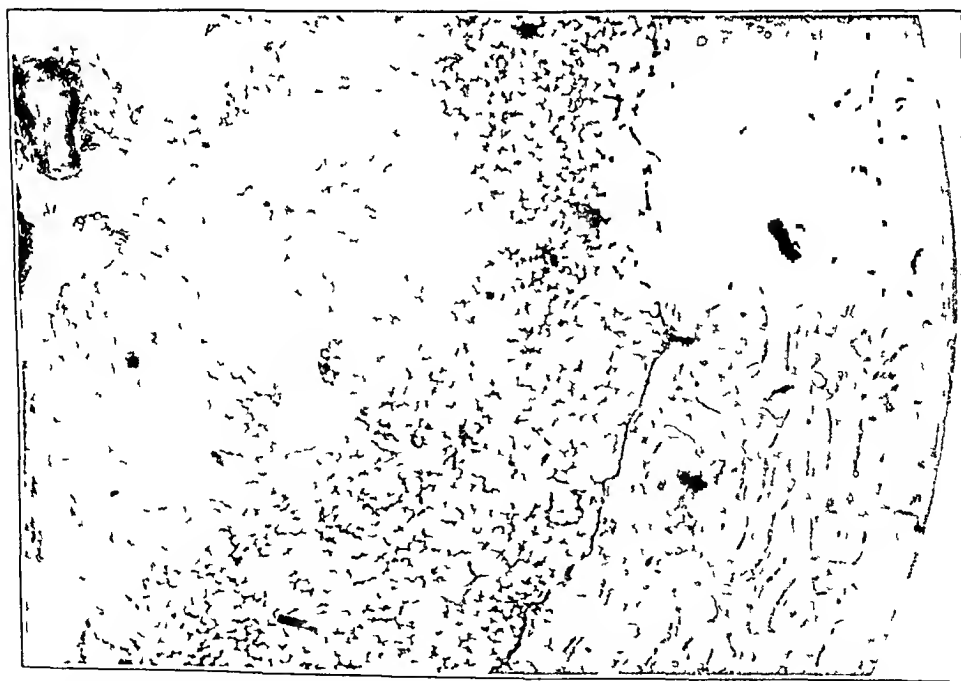


Fig 7—Photomicrograph ( $\times 18$ ) of bone from a dog which survived five months with complete biliary fistula.



any further secretion of bile salts is due to conversion of food into bile salts (the protein fraction, according to them) Whipple and his co-workers showed that the addition of fresh meat (liver, kidney or muscle) was the most potent in increasing the output of bile salts. On such diets the dogs excreted from 200 to 300 mg per kilogram per day. Considerably less effective was egg or milk protein, while on diets of pancreas and fish (including the salmon bread) the daily excretion usually ran about 100 mg per kilogram per day. Addition of carbohydrate had little or no influence on the output of bile acids, and on a purely carbohydrate diet the excretion stayed about the fasting level. Under these conditions the bile was highly colored, sticky and thin.

These findings in dogs with adjuvant feedings are strikingly different from those in our animals in which the deprivation of bile was total and a progressive emaciation was taking place. The average dog put out but 309 mg of bile acids per hundred cubic centimeters of bile, although the figures for the individual dogs at various times varied as much as 1,000 per cent. These huge unexplainable fluctuations are a commonplace finding in all studies on bile and necessitate prolonged averages in order that definite interpretations of any given phenomenon may be made. This average is only about from one half to one third of the normal content. If measured as amounts excreted per day the average is 456 mg per dog per day, a figure equally low. Most of Whipple's results are expressed as milligrams per kilogram per day, and the average of our entire series was 34.4 mg per kilogram per day. This lies within the fasting range or the range of "endogenous" bile salts, as reported by Whipple and his co-workers, and makes it clear that there is a much greater fall in the bile acid content of the bile than in its volume or in any other of its constituents. Here again we find the wide (tenfold) daily variations, but there is a very clear tendency for each dog to run on its own individual level. This has also been commented on by Whipple.

It is interesting, however, to note that there was no progressive fall in the acids of the bile as the emaciation progressed (tables 1 to 4). The values calculated in the early stages are comparable to those calculated later. Even in the terminal stages two of the dogs had higher concentrations of bile acids and a higher output of bile acids per kilogram per day than immediately after the operation. This is clearly indicative of the fact that there is no lack of this molecule in the body, and that it is impossible to assign lack of bile acids to a prominent place in the etiology of biliary cachexia.

It has been stated by some that administration of viosterol would increase the acids in the bile.<sup>66</sup> This was tried on two of our animals in the terminal stages (last month). One of these dogs had the highest

figures in tables 1 to 4 must be interpreted in this light. Nevertheless, even allowing for such errors in method, it is seen at once that there is most decidedly not a lack of sterols that could possibly be interpreted as "sterol starvation." The blood cholesterol tends to be slightly lower in the latter periods of cachexia, but significant falls are totally absent. In all the dogs the levels of blood cholesterol fell within the lower limits of normal, and in two of them a higher level was found during the last month of life than in the controls before operation.

The phenomenon of the *Esterius*, which recently was explained by Gardner and Gainsborough,<sup>83</sup> was not evident in our studies as the experimental periods were too short. It is well known that at the onset of either obstructive jaundice or biliary fistula there is a fall in the blood cholesterol, which later returns to a normal level and still later to levels about 50 per cent above normal. This is due to the loss of the absorbing power from lack of bile in the intestinal tract and to the consequent fall in the cholesterol esters to almost zero. The more recent work of Garside<sup>84</sup> on the other hand, showed a distinct rise in the early stages. The failure of our animals to show hypercholesteremia in the later stages of the cachexia is a point of special interest which will be noted later.

Further fluctuations in the later stages of the cachexia are probably related to periods of starvation from distaste for food. It has been known for many years that starvation is a most potent factor in raising the blood cholesterol, and this phenomenon is quite characteristic of so-called war edema and hunger edema. At any rate, there is no indication from any of our studies that the dogs at any time had hypocholesteremia.

The cholesterol in the bile showed similar fluctuations which are only in part accounted for. These changes are not related to changes in the rate of secretion of the bile or in its concentration, or to the rate of excretion or to the concentration of the bile salts. Figures 8 and 9 give a graphic representation of data gathered from tables 1 to 4. Whether one calculates the percentage of cholesterol in the bile or measures the amount secreted per day, it can be seen that the fluctuations are wide and apparently inexplicable. However, the curves in general do not show any evidence of lack of sterols in the organism. In some cases concentrations and rates of excretion are higher toward the end of the experiments, when the cachexia is extreme and in others they are lower. The concentration of cholesterol in the bile of the dog

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<sup>83</sup> Gardner, I. A., and Gainsborough, H. Blood Cholesterol Studies in Biliary and Hepatic Disease, *Quart J Med* **23** 465, 1930.

<sup>84</sup> Garside, E. Effect of Complete Biliary Fistula on Blood Cholesterol, *Proc Soc Exper Biol & Med* **28** 336, 1930.

readily absorbed. Evidence of synthesis of sterols in the body on any scale proportionate to the amounts daily excreted is totally lacking, but such a process on a very small scale cannot be denied. How important these small amounts may be is clear from a consideration of the fat-soluble vitamins and the profound physiologic events dependent on the presence of infinitesimal amounts of them. For a more complete discussion of these phenomena reference must be made to the elaborate studies of Windaus and of Wieland. Suffice it to say that no one has ever isolated from protein carbohydrate or fat any substance which in the least resembles the cholic acid radical fundamental to this group. How the plants manufacture sterols is not clear except for the undoubted fact that the yeasts build it out of carbohydrates. The reports of Whipple and his associates on the influence of carbohydrate in the decreasing of bile salts in the bile may have a bearing on this subject.

On the other hand, Smith and Whipple<sup>88b</sup> showed that ingestion of protein increases the acids in the bile and attributed this to an origin

TABLE 8—*Data on the Total Sterol Balance in Four Dogs for from Four and One-Half to Five Months Each*

Intake		Output	
	Bile acids (bile)		235.304
	Cholesterol (bile)		7.834
	Cholesterol (feces)		7.009
	Correction for about 25 per cent loss of feces		1,752 (estimate)
Total (food) 252,570 mg	Total		251.999

of the sterol molecule from the products of protein disintegration, assigning to the animal body an ability to synthesize these pyrrol ring products. It seems more logical to us to assume that the reason ingestion of protein increases the acids in the bile is that they are combined with either taurine or amino-acetic acid and that this is a method of eliminating these radicals.

In view of these facts it is interesting to study the sterol balance in biliary cachexia. Unfortunately our balance is not complete on account of the loss of stools, but a general idea may be arrived at and this loss allowed for, especially as the figure appears negligible in comparison with other far greater ones in the table (table 8). Allowance must also be made for the great inaccuracy of colorimetric methods of analysis as discussed. However, the very large number of estimations tend to balance themselves and at least partially to eliminate the error, and for this reason the average results should be best for study.

It can be seen that about 65 Gm. of sterol was ingested by our dogs in the experimental periods of from four to five months. Practically all the sterol is absorbable, as the amounts of sitosterol in bread are very

## RELATIONS TO PREGNANCY

One of the dogs (no 959) had a litter of seven premature pups on the seventeenth day after the experiment began, and an unusual opportunity was thus offered to study the much disputed question as to the relation of pregnancy to cholesterol metabolism. The much greater incidence of disease of the gall tract in women and its close association with the puerperium have long been known. More recently

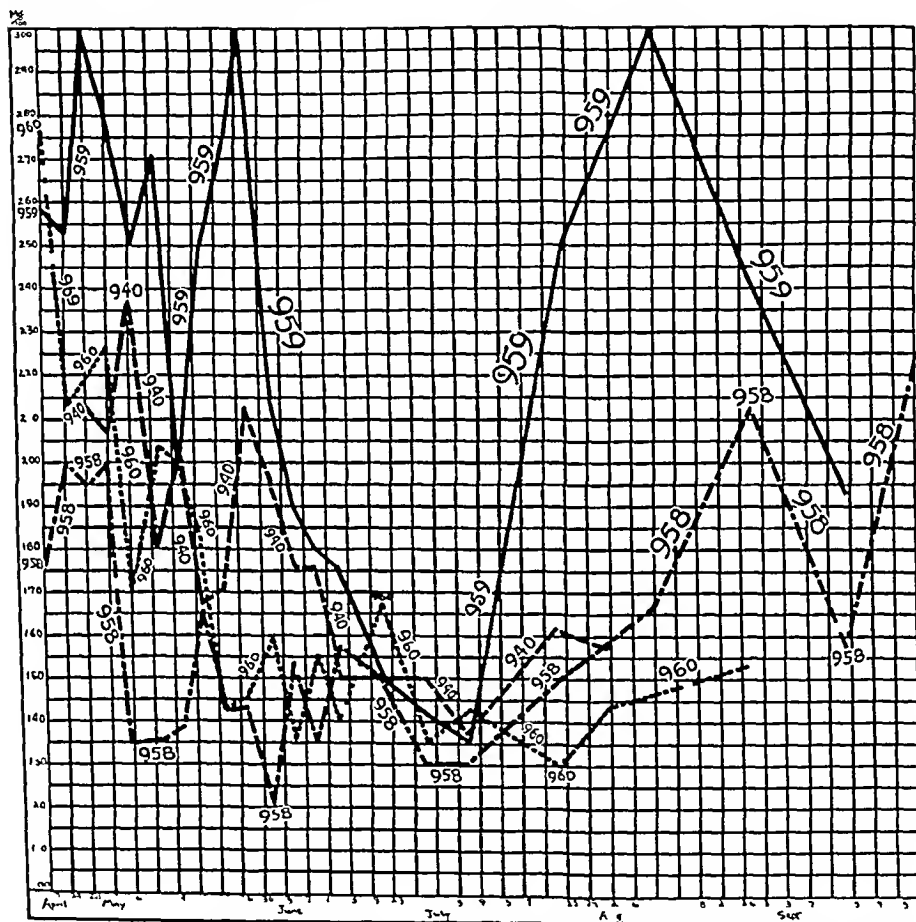


Fig 9—Graph showing the blood cholesterol curves of the dogs as given in tables 1 to 4. The dash line indicates dog 940, the dot and dash dog 958, the solid line dog 959, and the dotted line dog 960.

the association of pregnancy with hypercholesteremia appeared to complete the evidence and the attractive theory was offered that gallstones are caused by an overflow of cholesterol into the bile, with consequent crystallization of the supersaturated solution.<sup>85</sup> However, as has been

<sup>85</sup> McVee, I. W. Zur Frage des Cholesteringehalts der Galle während der Schwangerschaft, *Deutsche med. Wochenschr.* 39:994, 1913.

beyond doubt that cholesterol may be synthesized by the mammalian organism. If, then, our studies of balance appear to indicate that sufficient sterols have been ingested to account for all the excretion in the case of a biliary fistula, the suggestion may be made that in this condition the synthesis of sterols ceases as the results are far different from those in the normal person.

If, then, the sterol metabolism is at a standstill, except for the suggested oxidation of cholesterol into bile salts, a readily soluble and excretable substance, it seems that we have at hand a rational explanation of the close similarity of the manifestations of acholic cachexia and avitaminosis. It also explains why in the total absence of bile from the stools some observers have reported benefit from viosterol and others not, and why the ingestion or even injection of viosterol into the dogs in the present study was of no avail, there being no means to transport or use it even when injected.

The disturbances or total interruption of the enterohepatic circulation of bile salts in jaundice is tolerated far better than biliary drainage, and, according to this assumption, it should be

#### SUMMARY

A simple method of producing biliary fistula is described. By using this method we have had dogs survive considerably longer than they have after the use of any method previously reported on without adjuvant administration of bile, bile salts, liver, salmon bread, etc.

Anemia, osteoporosis or gastroduodenal ulceration did not develop.

The dogs did not manifest any lack of cholesterol or of bile salts in the body.

Their lives were not prolonged by the administration of vitamin D subcutaneously.

They did not exhibit "fat starvation."

Suggestive evidence is brought out that in the presence of a biliary fistula the bile salts are derived from the ingested cholesterol.

#### CONCLUSION

Acholic cachexia is not due to the absence of bile from the intestinal tract with consequent inability to absorb any specific food or vitamin. It is due to a disordered internal metabolism of sterols which inhibits proper utilization of them.

On the other hand, there was no corresponding increase in the bile secreted, nor was there any rise in the bile acids. The bile acids of the pregnant dog averaged 266 mg per hundred cubic centimeters, while three other dogs showed bile acid averaging 268, 346 and 453 mg, respectively. Thus, if anything, the level of the bile acids was lower although still easily within the limits of normal fluctuations. As a consequence there was an extended period in which the bile acid-cholesterol ratio was far below the critical point of 13. It has been previously reported by Andrews, Schoenheimer and Hrdina<sup>73</sup> that it took about 13 molecules of bile acids to hold 1 molecule of cholesterol in solution, and that if the ratio of the two was less than that figure, precipitation of the cholesterol was imminent. Unfortunately this bile was not examined for crystals before it was preserved in alcohol, as the chemical determinations were not made until after the conclusion of the experiment. These are the only figures that have come to our attention in which bile definitely supersaturated was secreted by the liver, as previous attempts to study this problem in dogs by variations in diet etc., had always shown that such a condition was due to the action of the gallbladder.<sup>20</sup>

The effects of pregnancy on the other observations were nil. The blood calcium, blood fats and general progress of the cachexia were unchanged. One other point, however, is worth noting. Immediately after the litter was born a moderate degree of anemia developed, possibly due to hemorrhage at parturition. Two days after delivery the red blood cell count was 3,240,000 and the hemoglobin content 70 per cent. Within five days the red cell count had gone up to 5,160,000 and four days later to 5,720,000. There was no such prompt regeneration of the hemoglobin. This seems a striking example of the ability of the dog with a biliary fistula to regenerate blood, even in the absence of any specific adjuvant, and has direct bearing on the problem of anemia previously discussed.

#### BILE SALTS

The output of bile salts of our dogs was considerably lower than that usually reported for animals which were well fed throughout the experiment. Whipple and his associates<sup>88</sup> showed that a dog kept in good condition by bile salmon bread etc. will put out from 30 to 40 mg of bile salts per kilogram of body weight per day under fasting conditions. This they assumed to be the "endogenous" bile salts, i.e., those derived from the breakdown of body proteins. They stated that

<sup>88</sup> (a) Smith, H. P., Groth, A. H., and Whipple, G. H. Bile Salt Metabolism. I. Control Diets, Methods and Fasting Output. *J. Biol. Chem.* **80**: 659, 1928.  
(b) Smith, H. P., and Whipple, G. H. Salt Metabolism. II. Influence of Meat and Meat Extracts. Liver and Kidney, Egg Yolk and Yeast in Diet, *ibid.* **80**: 671, 1928.

to Dr Van Horne, of Topeka, a general practitioner. He took roentgenograms and told her parents that she had a sarcoma. He prescribed roentgen ray treatments, which she received for over a year. She seemed to be getting worse, so she was finally taken to Dr Francisco, at Kansas City. Roentgenograms were again taken, but the diagnosis was bone cyst. Simple immobilization was instituted, first with a cast and later with a brace. About four and one-half years before the onset of the present illness she was pronounced cured, and the brace was discarded. She had no further trouble until the present illness. During this interval she was normal and active.

No important details were elicited in the family history of this patient. The parents were approximately 30 years of age when the child was born. Under the functional inquiry, it was noted that the patient was somewhat listless, drowsy and inclined to be "stupid" and that this was of recent development. No other points of any consequence were brought forth.

*Examination*—Physical examination revealed a fairly well developed girl, who was not acutely ill. She did not complain of pain directly. No deformities of the head were noticed, no tenderness was present over the sinus regions, no rash was present over the face or neck. The conjunctivae were slightly pale, the scleras were normal, the muscles of the eyes were normal. The pupils were round and equal and reacted to light and in accommodation. Examination of the ears and mouth did not reveal any pathologic condition, nor did that of the neck or chest. The heart and lungs were perfectly normal. Examination of the abdomen also failed to reveal any pathologic condition.

There was a peculiar, rather fusiform swelling of the right leg, from just below the knee to the middle third of the leg. There was definite but not severe tenderness to pressure in the region, the point of maximum tenderness being a little below the metaphysis. Swelling and tenderness were most prominent over the anteromedial aspect. The mass was not particularly warm but was perceptibly warmer than the other areas of the leg. It was not hard, yet not fluctuant or cystic. It was not soft, but rather of a semisoft consistency.

Examination of the urine revealed no definite pathologic findings. The examination of the blood showed 81 per cent hemoglobin, 5,730,000 red cells, 7,500 white cells and a normal differential count. The Wassermann reaction was negative, as was the Kahn reaction.

Anteroposterior and lateral roentgenograms of the leg showed an extensive process involving over half of the shaft of the right tibia. There was a peculiar woolly appearance of the bone as a whole. There was erosion of the tibia on the anteromedial aspect of the upper part of the shaft, just below the metaphysis. There was evidence of periosteal reaction, in certain areas a sunray effect could be made out, as if spicules were laid down at right angles to the line of bone.

The clinical diagnosis made by the orthopedist was osteogenic sarcoma of the right tibia. The roentgenologist, however, diagnosed the condition as low grade chronic osteomyelitis. The parents were advised of the discrepancy in the views of the orthopedist and roentgenologist and were urged to accept exploration. A conjoint meeting of the orthopedist, the roentgenologist and the pathologist was arranged to occur in the operating room the next day.

On Dec 20, 1934, a simple exploration was performed. Macroscopically the tissues resembled sarcomatous tissue rather than granulation (or cystic tissue). The roentgenologist stated that if the clinical and pathologic diagnosis was osteogenic sarcoma, the roentgenogram could be well interpreted as showing osteogenic sarcoma. A rapid frozen section was made by the pathologist (Dr J L Lattimore), who made a diagnosis of osteogenic sarcoma.

elevation of bile salts during the entire period and the other showed the lowest percentage of bile acids. In fact, this dog was the only one in which a profound terminal drop occurred.

The bile salt-cholesterol ratio as discussed here, except in the pregnant dog, in the range previously reported by us for dogs, i. e., from 30 to 70. This is considerably higher than that found in man, who usually has a bile salt-cholesterol ratio of from 20 to 40.<sup>89</sup> Thus it seems suggestive that when there is a disturbance in the metabolism of one constituent because of the biliary fistula the other is affected in about the same degree. The apparent excretion of one in the same ratio as the other suggests that there is a common origin and that the excretion of the two is in some way correlated.

#### THE STEROL BALANCE

The origins of the sterols in the body have been the source of considerable discussion. Any consideration of sterols must include with them the bile acids the chemical constitution of which is so similar in spite of the utterly different properties. A consideration of the accompanying illustration of the structural formulas of representatives of the two groups makes it clear that the relationship is a close one. It might be expressed by saying that bile acids are the corresponding fatty acids of the sterol monohydric alcohols (although this is not a strict relationship). Furthermore, it seems that, as a catabolic phenomenon, the bile acids might be expected to be derived from the cholesterol by some process of oxidation. This possibility is further supported by the fact that while no bile acids are ingested in the ordinary course of events, most diets contain an abundance of sterols.

While the intricacies of sterol metabolism cannot be discussed here, a few salient points may be brought out. One often wonders why the term "sterol metabolism" is used when nothing is known of any changes that occur in the molecule after absorption, except for the finding of di-hydrocholesterol in the stools after ingestion of other sterols. No products of the oxidation of sterols have ever been recognized and no substances found which may be looked on as building stones in its synthesis. From the series of studies of Schoenheimer<sup>90</sup> it is clear that plant sterols are totally unabsorbable from the mammalian gastrointestinal tract. However, if they are irradiated (as ergosterol) rapid absorption takes place. Ingested sterols of animal origin may be

89 Andrews, Schoenheimer and Hrdina.<sup>73</sup> Neuman, C. E. *Beitrage zum Studium der Gallenniederschläge und Gallensteinbildung*, Beitr. z. path. Anat. u. z. allg. Path. **84** 187, 1931. Ravdin, I. S., Riegel, C., Johnston, C. G., and Morrison, P. J. *Studies in Biliary Tract Disease*, J. A. M. A. **103** 1504 (Nov. 17) 1934.

90 Schoenheimer, R. *Newer Contributions to Sterol Metabolism*. Science **74** 579, 1931.



pathologist stated that grossly the tumor was of an irregular, fusiform shape and measured 18 cm in total length and 8 cm in width at its greatest diameter. It was covered by the deep or vaginal fascia, which apparently formed an uninterrupted thick capsule over the underlying tumor. On the anterior aspect of the tumor there was a surgical incision about 5 cm in length, and from the incision the neoplastic tissue was bulging out. In cutting the section, the knife encountered resistance, like that offered by cartilage. The surface of the section was grayish red, with a transparency similar to that of articular cartilage. No large vessels were present, and the tissue showed few hemorrhagic areas which could be attributed to vessels in the tumor. When the bone was cut longitudinally, the tumor was seen to extend from the metaphysis (which itself seemed to have been the site of an old fracture) downward to the segment corresponding grossly to the

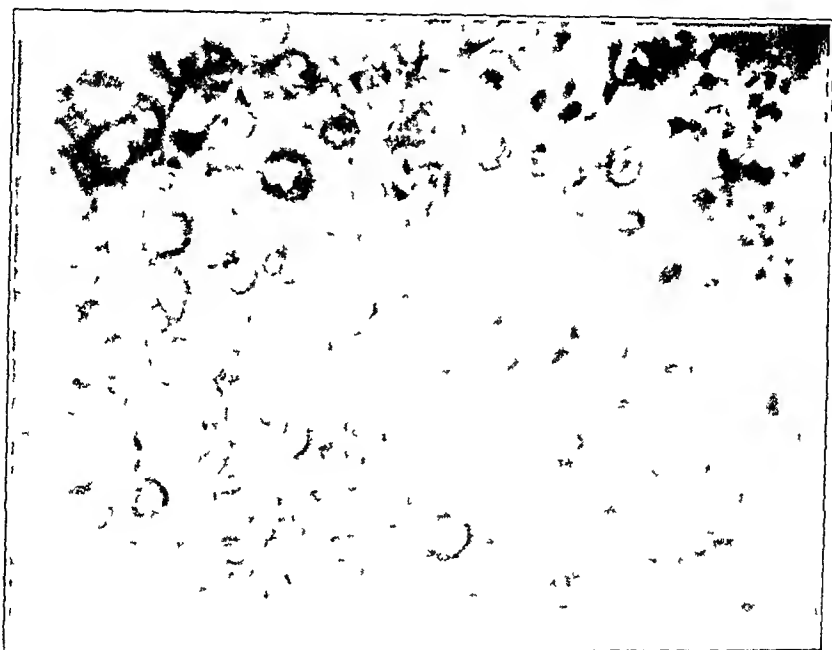


Fig 2—A high power photomicrograph of the section made from the tissue

distal margin of the middle third of the bone. However, the medullary canal presented an extension of the tumor below the margin just described.

Although the periosteum seemed intact, particularly at the upper limit of the tumor, in the vicinity of the metaphysis, it seemed in direct continuity with the tumor tissue, and no separation of the two was possible in this locality. Also in the metaphyseal region, the bone was soft and rarefied, and in its central portion it could be scraped out with a knife. This was probably the zone which had given the impression of a bone cyst in the roentgenograms. Figure 1 illustrates various views of the gross specimen, including a longitudinal section through it.

*Microscopic Examination*—Under the high power of the microscope, the tumor tissue was found to be made up chiefly of large capsulated cells, which had the characteristics of hyaline cartilage cells. There was no uniformity in the size of the cells, so that in the same field one could see very large cells with rather large nuclei and small cells with pyknotic nuclei. Two nuclei were often observed in

small and the sterols are mostly derived from the laird used in its manufacture. In this period, there were excreted in the bile about 2 Gm and in the stools about the same amount, which should probably be doubled or tripled to allow for losses. This is especially true if one recalls Sperry's<sup>91</sup> experiments indicating that the amount of cholesterol in the stools is increased in the presence of a biliary fistula on account of incomplete absorption. Furthermore, our estimations of cholesterol were made by a colorimetric method which did not show the coprosterol which makes up much of the fecal lipoids. Against this then, one may balance the loss of bile acids to the extent of about 59 Gm which comes remarkably close to the establishment of a balance. One is tempted to assume that this amount of ingested cholesterol has been converted into bile acids.

If this is true the direct implication is that in the presence of biliary fistula at least the body does not synthesize sterol, neither cholesterol nor bile acids. The importance of this may not be very great. If the synthesis of sterols ceases, it is clear that the metabolism of this molecule is at a standstill. Considerable evidence is at hand<sup>83</sup> that the form of cholesterol and other absorbable sterols is not unchanged within the body. The conversion of the inactive ergosterol into the active form by sunlight is simply a change in isomerism, and many observers believe that comparable changes in the body sterols take place, and that the cholesterols found in the blood, bile, cell walls, etc., are not by any means identical optically, even if they are chemically, which in turn is uncertain. Even the transport of such substances within the body is difficult to understand in view of their extreme insolubility not only in water but in most body fluids. In bile they are held in solution, as Andrews, Schoenheimer and Hrdina<sup>73</sup> have shown, in a chemical combination with the bile salts. In the blood protein is probably the carrier (Cholesterol is insoluble in blood and a chemical combination appears necessary). Recent studies by Gardner and Fox,<sup>92</sup> Thannhauser and Schaber,<sup>93</sup> Beumer and Lehmann<sup>94</sup> and Randles and Knudson<sup>95</sup> showed

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91 Sperry, W. M. Lipid Excretion. IV. A Study of the Relationship of Bile to the Fecal Lipids with Special Reference to Certain Problems of Sterol Metabolism, *J Biol Chem* **71** 351, 1927.

92 Gardner, J. A., and Fox, F. W. On the Origin and Destiny of Cholesterol in the Animal Organism. XII. On the Excretion of Sterols in Man, *Proc Roy Soc London, sB* **92** 358, 1921. Fox, F. W. The Origin and Destiny of Cholesterol in the Animal Body. XIV. The Cholesterol Metabolism in Normal Breast Fed Infants, *ibid* **98** 76, 1925.

93 Thannhauser, S. J., and Schaber, H. Kann der tierische Organismus Cholesterin synthetisieren? *Ztschr f physiol Chem* **127** 278, 1923.

94 Beumer, H., and Lehmann, F. Ueber die Cholesterinbildung im Tierkörper, *Ztschr f d ges exper Med* **37** 274, 1923.

95 Randles, F. S., and Knudson, A. Studies on Cholesterol. I. Synthesis of Cholesterol in the Animal Body, *J Biol Chem* **66** 459, 1925.

It was noted that when the child was nine months old she slipped and fell, receiving a definite injury to the leg. Although the parents stated that there may have been some deformity at that time, this is questionable. Certainly, it was not deformity but pain which made them suspicious. Conservative treatment was tried for six months, but had no effect in lessening the pain. The child was therefore taken to Dr. Van Horne, at Topeka, when she was 15 months old. Roentgenograms at that time caused Dr. Van Horne to make a diagnosis of sarcoma, but his

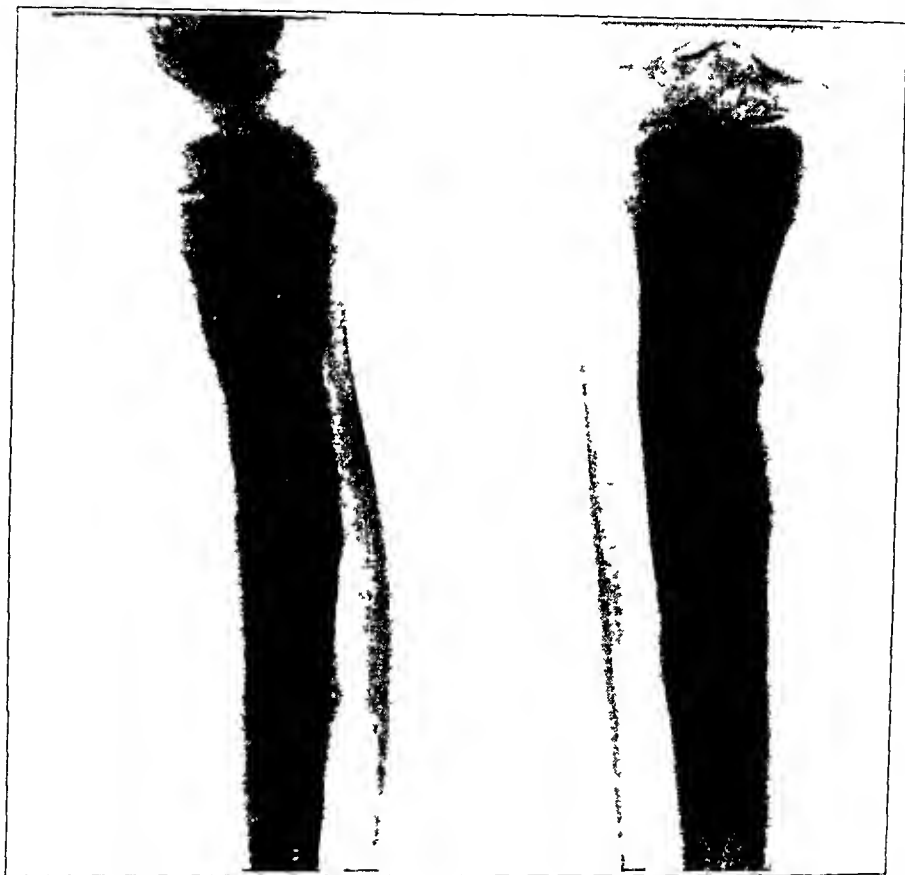


Fig. 4—The final anteroposterior and lateral views, taken Dec. 19, 1934, when the tumor was diagnosed finally as an osteogenic sarcoma.

description to the parents was so characteristic ("the roentgenograms showed a soap-bubble effect in the upper end of the bone") that one does not doubt that he saw the same picture which Dr. Francisco found later. Roentgen ray treatment had no effect in controlling the condition, and again the symptom which caused them to seek further help was pain. No definite deformity was described at that time.

The child was approximately 3 years old when she was first seen by Dr. Francisco, and at that time no gross deformity was noted. There

# MALIGNANT DEGENERATION OF A BENIGN BONE CYST?

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The following case is reported for several reasons. First, as far as we could ascertain a malignant change in a benign bone cyst has never been reported in the world literature. Second, a benign bone cyst in a child before it has begun to walk is a rarity. Third, team-work between surgeon, pathologist and roentgenologist and also between surgeon and surgeon is a necessity in developing the complete history and progress of an individual case.

## REPORT OF A CASE

*History*—I M, aged 9 years, was referred to the clinic of Dr Pusitz on Dec 18, 1934, by Dr Brethauer of Alta Vista, Kan, with the essential complaint of pain and swelling in the upper part of the right leg.

The history was that about three months before, while playing with other children in school, she was kicked on her leg. She did not have any immediate trouble, so the incident was forgotten. Shortly after this, however, she began to complain of slight pain, especially after being on her feet any length of time. In fact, the pain was present only when she walked. Rest gave relief. There was no pain during the night, and she slept well. The weather had no definite effect on the condition. About one month before she came to the clinic, she was seen by her family physician, who detected some swelling in the upper part of the right leg. This had not increased much in size. Whereas formerly she had always been a rather active child, she seemed to have lost her "pep." There had been no chills or fever. During the last week or so the tumor had become perceptibly warm. Because it was believed that she possibly had an infection of the bone, she was referred to the orthopedic clinic at Topeka.

She had had the ordinary diseases of childhood. At the age of 9 months, when she was beginning to walk, she slipped on a wet floor and hurt her leg. She complained of pain, but there was no swelling at the time. There was some slight deformity. The family physician told her parents that there might be a crack in the bone. The pain later became a prominent symptom, especially after she had tried to walk for some time. Because the pain increased in severity, she was taken

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From the service of the Kansas Crippled Children's Commission

Callus is the result of a productive process. Clearly, along with this productive phenomenon there must be a retrogressive or absorptive change to give a cystic appearance. If this had been such a change, one would hardly expect the contour of the bone to be so regular, and certainly in the early stages there would have been evidence of a break. But it was not until June 7, 1928, that definite evidence of a pathologic fracture was seen. Even the parents cannot say certainly that there was definite deformity prior to this.

Benign chondroma may be considered only to be dismissed. In the first place, this tumor has an entirely different distribution than has a benign bone cyst. The growth is rare in persons under 20 years of age. The clinical symptoms are never severe. It is practically restricted to the small bones of the hands and feet and to the articular regions of the spine and the sternocostal joints. The roentgenogram shows a small translucent area of rarefaction. The cortical bone about the lesion is thinned and expanded. Pathologic fracture occurs in 10 per cent of the cases. Productive changes are rare.

The early stages of the condition in the case reported here certainly were not those of an osteogenic sarcoma and this is proved by the progress of the case up to the discharge of the patient by Dr. Francisco in 1930.

There are two other possible conditions, namely, benign bone cyst and giant cell tumor. Bone cyst is a form of osteitis fibrosa<sup>2</sup> (although this statement should be modified) and is usually found in just the location described in the case in question. It is usually a solitary osteolytic tumor occurring in a patient under 20. In the early stages giant cells are noted in the bone tissues, pathologic overactivity of these cells for some reason or other resulting in the formation of the cyst. When the phase of bone destruction ceases a stage of bone production ensues, especially about the periphery of the tumor. These two phases may overlap. The proliferation of the adjacent cortex and of the subperiosteal layer of osteogenic tissue (or the cambium of the periosteum) wall in the area of cystic activity. In multilocular cysts, the very walls of the subdivisions seem to have this power as is evidenced in the roentgenograms (fig. 3). Especially is this process of proliferation enhanced when a pathologic fracture occurs. This seems to hasten the process to complete obliteration.

Although Geschickter<sup>2</sup> considered the benign bone cyst to be a variant of the giant cell tumor which has healed or is healing there are certain distinct fundamental clinical and radiologic differences.

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<sup>2</sup> Geschickter, C. F., and Copeland, M. M. Tumors of the Bone, New York, American Journal of Cancer, 1931. Recurrent and So-Called Metastatic Giant Cell Tumor, Arch. Surg. **20**: 713 (May) 1930.

As an unquestioned diagnosis was desired, and because roentgenograms of the lungs were desired by the orthopedist, it was decided to do a simple biopsy for the present and to amputate later. Since the patient had been under treatment by Dr. Francisco, he was called into consultation.

The history of the case had not been given as clearly as it has been presented in this outline, but with the additions made by Dr. Francisco, the complete history was available. His impression was that the tumor resembled an osteogenic sarcoma, but he thought it well worth while to delay amputation so that Professor Wahl could make a pathologic study, since the tumor had been benign before. Also he would hesitate before calling it malignant since he could not recall any case of malignant change in a benign bone cyst.

The reports from Professor H. R. Wahl, of the University of Kansas, Dr. Michele Gerundo, of the Topeka State Hospital at Topeka, Kan., and Dr. J. L.

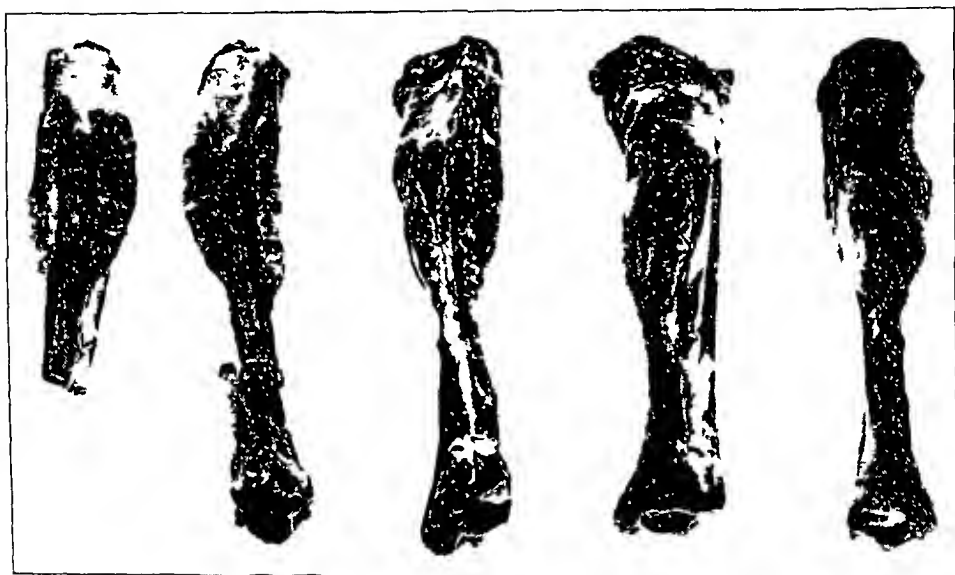


Fig. 1—Various views of the macroscopic specimen carefully dissected clean from the overlying tissue. From right to left a medial view, a posterior view, a lateral view and a view of longitudinal sections, the section being made antero-posteriorly through the entire specimen.

Lattimore, pathologist, were unanimous in pronouncing the section that of an osteochondrosarcoma.

The final diagnosis was therefore osteogenic sarcoma and immediate amputation to be followed by irradiation was advised. The amputation was performed in the upper part of the thigh at the junction of the upper with the middle third, leaving just enough stump to control an artificial leg. The patient did exceptionally well after the amputation and has made a remarkable personal change. She received her first course of roentgen therapy and is to return for further irradiation under the supervision of the radiologist.

**Macroscopic Examination**—The gross specimen was dissected out carefully after the amputation. A tumor was found involving the upper half of the tibia, extending all around the bone, but most apparent on the anteromedial aspect. The

were no areas of cyst formation or of giant cells. Geschickter made the statement that there has never been reported a proved case of malignant degeneration following a benign bone cyst. He even denied the possibility of malignant degeneration following a giant cell tumor. He had at his disposal a wealth of material with all possible variations. It is difficult, therefore, to deny his statement and try to prove the contrary. Therefore, the case is left for future digestion and analysis, and the material will be placed at the disposal of the registry.

#### SUMMARY

A completely studied case is presented in which a chondrosarcoma arose at the site of a former benign bone cyst.

There are two rare features. First, the fact that the formation of cysts began when the patient first started to walk, and second, the malignant degeneration of the cysts.

one capsule. Around such zones there were numerous cells of the same type, but growing without capsules, and other cells which showed a transition toward the fibrous type of cell. In these areas blood vessels were absent. In other zones a mucous degeneration of tumor cells was present, which gave the tumor a pseudomyxomatous appearance. The stroma formed by a dense fibrous tissue, which in some places was difficult to distinguish from the tumor tissue itself, contained few vessels and some occasional hemorrhagic areas. It seemed to originate from the fascia, the prolongations of which, penetrating into the tumor tissue itself, gave to it a coarse lobulated appearance. Many cells were observed in various stages of division, and numerous mitotic figures were noted. Figure 2 illustrates a section of the tumor tissue highly magnified.

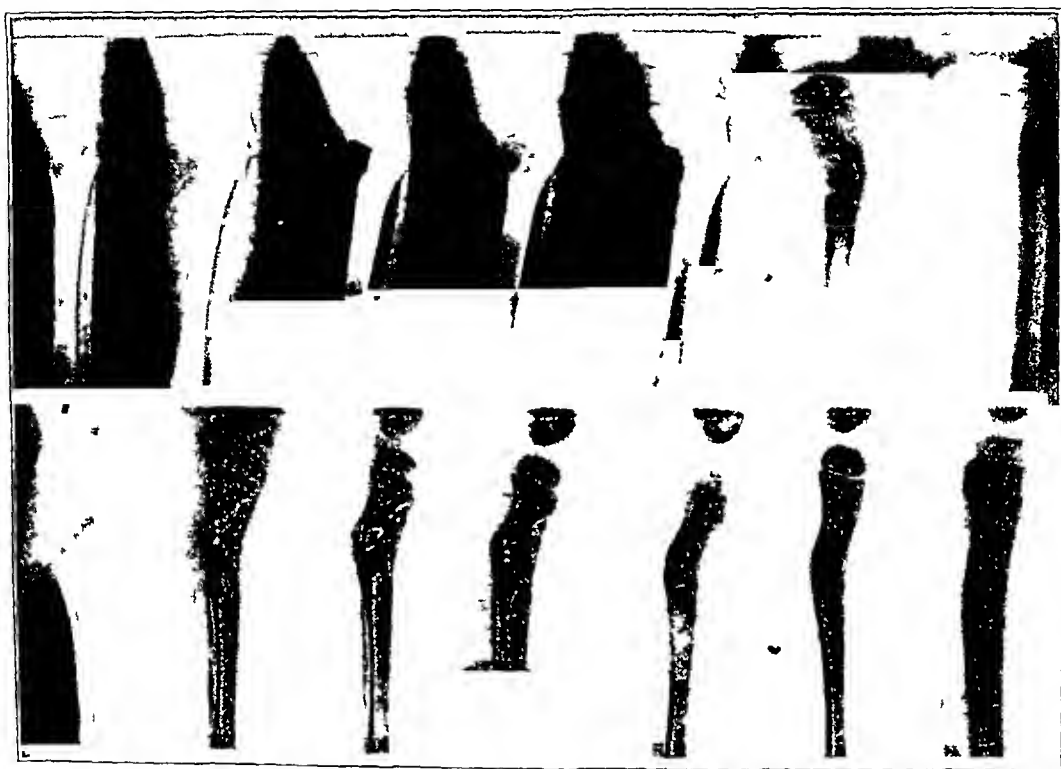


Fig 3—Comparison roentgenograms. In the upper row are the anteroposterior views in chronological order, in the lower row are the lateral views in chronological order.

The pathologic diagnosis was chondrosarcoma of the tibia originating from the metaphysis and extending to the diaphysis of the bone.

#### COMMENT

Although there are gaps in the history of this case from the material collected from the family physician, the orthopedic surgeons and the parents (the general practitioner who took the first roentgenograms is dead) one can form a fairly good concept of the case as a whole.



As the result of his clinical studies, Georg Wolfsohn<sup>4</sup> expressed the belief and presented some evidence to show that the incidence of carcinoma in patients with gastric ulcer not treated surgically is considerably higher than in those treated by simple gastro-enterostomy. He argued that even though an ulcer is not removed or even completely healed as the result of the operation, gastro-enterostomy, in some manner not clearly understood, affords a certain degree of protection against the later development of carcinoma.

With regard to gastro-enterostomy for duodenal ulcer, reported instances of gastric carcinoma developing after the operation are exceedingly rare. In a study of the end-results of gastro-enterostomy in 500 consecutive cases of duodenal ulcer Balfour<sup>2</sup> found no instance of carcinoma developing subsequent to the operation as the cause of any of the late deaths in his series.

After an extensive search of the literature, I have been able to discover only five reports of carcinoma of the gastrojejunal stoma following operation for chronic duodenal ulcer. By far the most comprehensive case report and discussion of the matter appeared in 1932, in a paper by Singer.<sup>5</sup>

Singer, in discussing the relationship between gastro-enterostomy and the subsequent development of carcinoma of the stomach, presented a detailed report of a case of carcinoma of the gastrojejunal stoma occurring in a 64 year old man twelve years after a pylorotomy and posterior gastro-enterostomy for chronic duodenal ulcer. At the time of the original operation, the patient was found to have, in addition to the duodenal ulcer, chronic cholecystitis with extensive adhesions in the neighborhood. Accordingly, in addition to the pylorotomy and gastro-enterostomy, a cholecystectomy with lysis of adhesions was performed. There was complete relief from symptoms for one year following the operation, after which the patient began to suffer from a recurrence of his symptoms necessitating a strict dietary regimen. In spite of this the symptoms gradually increased. Roentgen examinations repeatedly revealed a filling defect on the greater curvature in the distal third of the stomach, and the diagnosis of carcinoma of the gastrojejunal stoma was suggested by the roentgenologist. A laparotomy disclosed a soft, irregular mass in the region of the anastomosis. The gastro-enterostomy anastomosis was eliminated, the portion of the stomach containing the tumor was resected and the operation was concluded according to the Billroth II method. Death occurred two days later.

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<sup>4</sup> Wolfsohn, Georg. Ueber Magenkarzinom nach Gastroenterostomien wegen Ulkus. *Deutsche med. Wchnschr.* **54** 1079 (June 29) 1928.

<sup>5</sup> Singer, Harry A. Carcinoma of the Gastrojejunal Stoma Following Operation for Peptic Ulcer, *Arch. Int. Med.* **49** 429 (March) 1932.

is available the clinical history of the case from then until June 25, 1930. Dr. Francisco's series of roentgenograms, along with those taken in Topeka in December 1934, are illustrated in a comparative manner in figure 3.

Anteroposterior and lateral roentgenograms of the right tibia, taken on April 4, 1928, showed a multilocular cystic appearance of the upper end of the tibia. This began at or just below the metaphyseal end of the diaphysis and did not extend upward at all, so that the lesion did not affect the epiphyseal line. Areas of sclerosis were seen already lining some of the cystic cavities. The area of involvement extended downward for about one-third, or less, of the length of the shaft of the bone.

Similar views taken June 7, 1928, showed somewhat the same features except that there seems to have been a mild pathologic fracture. The anterior wall of a large cystic area at the extreme anterior portion of the bone had been entirely absorbed. There was a sort of buckling in this region, causing an effect of hyperextension. The pathologic condition, however, was all below the epiphyseal line. There was much evidence of bone production, although the process did seem to have extended downward slightly. There was definite evidence of a pathologic fracture at that time. The parents also stated that from that time on they noted deformity in the upper part of the leg.

The roentgenograms taken on Sept. 22, 1928, showed still further condensation of bone, and those taken on Jan. 21, 1929, indicated a continuation of the process. The same may be said of those taken on Aug. 6, 1929. On June 25, 1930, the roentgenograms showed almost complete obliteration of the cystic cavities, with much condensation of the bone. It was at that time that the patient was discharged by Dr. Francisco as cured of the bone cyst. No further trouble was encountered until the present illness began.

#### DIFFERENTIAL DIAGNOSIS

If it were not for the malignant termination of the case, the only tenable diagnosis would be benign bone cyst. However, certain conditions must be thought of in the differential diagnosis, although in our opinion they can all be ruled out in favor of benign bone cyst.

Going back in the history, we found that a trauma of fairly severe nature had been sustained by the child. The question comes up as to whether or not she had a fracture at that time. Continental writers,<sup>1</sup> especially Italian, have spoken of a "softening of callus" which may result in areas of absorption so as to simulate the formation of cysts.

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1 Jeanneney, G. *Les tumeurs des os*, Paris, Masson & Cie, 1932. Uffreduzzi, O. *Trattato di patologia chirurgica generale e speciale*, Torino, Unione tipografica editrice Toinese, 1933, vol. 1.

lumen Microscopically it proved to be carcinoma, and there were metastases in the liver, esophagus and regional lymph nodes

Beatson<sup>9</sup> reported the case of a 52 year old man who came under observation with the complaints of vomiting, diarrhea, epigastric pain and abdominal tumor Eleven years previously a gastro-enterostomy had been performed for a "dilated stomach" (possibly due to a pyloric ulcer) He was well for eight or nine years, after which his health began to fail A second laparotomy was performed, and a carcinomatous mass was found on the lesser curvature, stretching down the posterior wall and involving the new gastro-enterostomy opening Owing to the presence of metastases, nothing was done He died twelve years after the first operation Necropsy showed a firm mass occupying the pyloric portion of the stomach The gastro-enterostomy stoma was surrounded by the ulcerated new growth, with obstruction of the efferent jejunal loop Microscopically the lesion proved to be an adenocarcinoma of the stomach

Beatson offered two possible interpretations of the findings in this case The first assumed that the original gastro-enterostomy was done for pyloric obstruction due to a gastric ulcer near the pylorus and that subsequently this ulcer had become malignant and in the course of its growth had extended into the gastro-enterostomy opening His second explanation was that the malignant lesion had started in the wall of the gastro-enterostomy wound on the gastric side and by extension had involved the pylorus The first view seems the more tenable

To the cases just cited I am able to add a verified case of carcinoma of the gastrojejunal stoma occurring in a man of 49 seven years after a von Eiselsberg exclusion operation for chronic duodenal ulcer

#### REPORT OF A CASE

*History*—Mr T T, a Czecho-Slovakian factory worker aged 42, was admitted to the University Hospital on Aug 8, 1927, with the complaint of "pain in the stomach" The family history was excellent, there being no history of malignant disease The past history of the patient was essentially unimportant The patient had enjoyed good health until about one and one-half years before admission to the hospital, when he began to be troubled with severe epigastric pain, which became progressively worse The pain usually started in the right lower quadrant and radiated to the right upper quadrant and over to the midline Frequently it began in the epigastrium and radiated to the right lower quadrant The pain came on from one to one and one-half hours after meals and was often followed by vomiting, which afforded some relief He was unable to say whether food or soda would relieve the pain There had been a loss of weight of 24 pounds (10.8 Kg) during the preceding few months

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9 Beatson, George T Carcinoma of the Stomach After Gastrojejunostomy, Brit M J 1 15 (Jan 2) 1926

First, a giant cell tumor is a solitary osteolytic tumor occurring in adults rather than in the younger groups. It is a progressive type of lesion and shows in the roentgenogram as a circumscribed, bone-destructive lesion occurring in the epiphysis. It usually shows a globular, trabeculated area of rarefaction, which is asymmetrical in position. It usually begins subcortically at one side of the epiphysis and gradually works its way toward the center, affecting the cancellous bone as it does so. Therefore, even though the histologic history of the benign bone cyst and that of the giant cell tumor may usually be the same, clinically and roentgenologically they are different. It is important to note that roentgen ray therapy has a remarkable effect on a giant cell tumor, whereas it does not have this marked effect on a benign bone cyst. Certainly the progress in this case would favor the diagnosis of benign bone cyst rather than one of giant cell tumor.

#### TREATMENT

It seems to us that the most important element in treatment is to enhance the proliferative activity. While roentgen ray therapy seems to act very well in certain cases of giant cell tumors, it seems too variable in its effect on bone cysts. Recently one of us had a chance to study the pathologic changes in a series of cases of bone cyst in four different clinics. While no statistical outline was made it was noted that roentgen ray therapy did not give good results in treatment. In the cases in which pathologic fracture had occurred, the end-results were uniformly good but the time factor was variable, as a rule being very much prolonged. In this case, of course, simple immobilization had been instituted. The best results, however, seemed to follow operation in which curettement or curettement with application of a graft, was adopted. Here the results seemed very good, and the time required for complete obliteration of the cystic cavities was much less than with the other methods of treatment.

#### PROGNOSIS

The prognosis is usually excellent for complete obliteration of the cystic cavities. However in certain cases years may be required before the terminal healed stage is reached. Recurrence is more frequent with conservative treatment than with surgical intervention. In the case reported, it is definitely known that the cyst was still present over four years after it was first observed. During this stage there were active young osteogenic cells claiming the picture. Can these cells assume malignant characteristics? Certainly in this case if the previous history had not been carefully and accurately obtained, the diagnosis of bone cyst might have been denied. Especially might this be true since the pathologic section showed the typical picture of chondrosarcoma. There

*Pathologic Report*—A lymph node removed from the region of the stomach was reported by Dr A S Warthin as showing "chronic lymphadenitis, acute congestion and edema but no neoplasm"

*Second Admission*—On May 18, 1934, the patient returned with the complaint of abdominal pain, vomiting, diarrhea, weakness and loss of weight

He had remained well after his discharge from the hospital until the fall of 1933 (six years). During this time he had gained considerable weight, was able to work and had been entirely free from symptoms. He had adhered to the prescribed diet for several months and then began to eat without restriction. In the fall of 1933 diarrhea suddenly developed, the stools numbering from ten to twenty a day. In addition to this, for the three weeks before admission, there had been a dull aching epigastric pain accompanied by vomiting. The pain had



Fig 2—Sketch made at the time of the second operation, showing the carcinoma situated at the gastrojejunal ring. The carcinoma completely encircles the stoma and is limited to the gastric side of the junction, the jejunum remaining uninvolved. The insert shows diagrammatically the nature of the original operation performed in 1927.

been aggravated by food. Finally he had been able to tolerate only small quantities of milk and water. He had lost 29 pounds (13.1 Kg) in weight since these symptoms had been present.

*Examination*—There was evidence of considerable loss of weight, moderate emphysema and an abdominal tumor attached to the old scar left by an upper right rectus incision. The mass seemed to be about the size of a small orange and moved downward with respiration. It was hard and firm and felt somewhat nodular. In the left upper quadrant the outline of the distended stomach could be clearly made out. There was definite resonance on percussion over this area.

The Kahn reaction of the blood was negative. A blood count revealed hemoglobin, 75 per cent (Sahli), erythrocytes, 4,550,000, leukocytes, 5,800. The

# CARCINOMA OF THE STOMACH FOLLOWING GASTRO-ENTEROSTOMY FOR PEPTIC ULCER

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The development of carcinoma of the stomach after a gastrojejunal anastomosis for chronic peptic ulcer is, on the whole unusual. Its occurrence has been observed chiefly in certain cases of gastric ulcer for which gastro-enterostomy had been performed when, because of the great size, inaccessible location or extensive fixation of the lesion, its removal would have been an excessively difficult and hazardous undertaking. It is the consensus of most present-day writers in considering the life history of gastric ulcer that approximately 5 per cent of these benign ulcers will ultimately undergo malignant degeneration if they are not healable when treated by dietary or other nonsurgical measures. It therefore seems reasonable to assume that, likewise gastric ulcers which fail to heal after an indirect type of operation such as gastro-enterostomy, should show similar tendencies. Jean Varnier<sup>1</sup> estimated that carcinoma will ultimately develop in from 2 to 5 per cent of the cases in which gastro-enterostomy is performed for gastric ulcer. Some evidence on this score may be obtained from a study of the statistics from the Mayo Clinic.<sup>2</sup> There it has been found that in the cases of gastric ulcer dealt with by gastro-enterostomy alone the death rate during the five year period following operation was two and one-half times as great as the death rate in a similar number of persons in the general population. Likewise during the first year after operation the death rate was 17 per cent in the group of patients with gastric ulcer in contrast to 5 per cent in the group of patients with duodenal ulcer treated by gastro-enterostomy.<sup>3</sup> It seems probable that malignant transformation is responsible, in part at least for this higher death rate in the patients with gastric ulcer.

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From the Department of Surgery, University of Michigan

1 Varnier, Jean. Le cancer de l'estomac chez les ulcéreux gastriques opérés par gastro-enterostomie, *Paris med* 2 93 (July 29) 1933

2 Balfour, Donald C. Results of Gastro-Enterostomy for Ulcer of the Duodenum and Stomach, *Ann Surg* 92 558 (Oct) 1930

3 Horslev, J. Shelton, and Horslev, John S., Jr. Surgical Diseases of the Stomach, in Graham, E. A. Surgical Diagnosis Philadelphia W. B. Saunders Company, 1930, vol 2, p 553

differential count showed polymorphonuclears, 55 per cent, basophils, 1 per cent, eosinophils, 1 per cent, lymphocytes, 39 per cent, mononuclears, 4 per cent. The color index was 0.82. The red cells appeared normal. The platelets were normal in number. The urine was normal aside from a faint trace of albumin. The stool gave a positive reaction to the benzidine test but was otherwise normal. Examination of the gastric contents revealed no free hydrochloric acid after the injection of histamine.

The report of a roentgen examination on May 21, 1934 was "There is marked gastric retention with a constant filling defect in the lower portion of the stomach, giving the impression of neoplasm in the distal third of the stomach causing gross obstruction" (fig. 1).

The clinical diagnosis was (1) marginal ulcer or (2) carcinoma of the stomach obstructing the gastro-enterostomy stoma. Operation was advised.

*Operation*—Operation was performed on May 26, 1934 (H. K. R.). Tri-bromethanol in amylene hydrate and ether were used for anesthesia. The palpable mass was found to involve the distal portion of the stomach, the upper half of the stomach being essentially normal. The greater portion of the tumor lay behind the transverse colon and was intimately attached to the liver and the gallbladder (fig. 2). It was mobilized, and the gross appearance suggested a scirrhus carcinoma. It seemed to originate from the wall of the stomach and ended abruptly at the point where the stomach and jejunum had been joined at the former operation. It completely encircled the stoma and thereby produced considerable obstruction at the outlet of the stomach. There were no metastases, and the fixation to the liver and gallbladder was thought to be inflammatory. The lower portion of the stomach, including the entire mass, was resected and also the segment of the jejunum involved in the old anastomosis. An end-to-end anastomosis was then done between the ends of the jejunum, and the mouth of the remaining gastric pouch was reanastomosed to the side of the jejunum just distal to this end-to-end anastomosis. The stump of the duodenum was found buried in old adhesions. There was no evidence of abnormality at this point, and accordingly it was not disturbed.

*Postoperative Course*—The convalescence was uneventful, and the patient was discharged from the hospital on June 12, 1934.

*Pathologic Diagnosis*—The pathologic diagnosis given by Dr. J. C. Bugher was "Advanced scirrhus carcinoma infiltrating entirely through the stomach wall, marked hyperplastic gastritis and subserosal carcinomatous infiltration. The portion of intestine shows chronic catarrhal inflammation with some hyperplasia of the mucosa. There is no carcinoma on this portion" (figs. 3 and 4).

*Subsequent Course*—It has been impossible to follow the subsequent course in this case, as the patient has never returned to the clinic since his discharge, and letters to him have been returned unanswered.

#### COMMENT

This case seems similar in many respects to the one reported by Singer. As in Singer's case, well marked chronic hyperplastic gastritis with occasional areas of polypoid overgrowth was present, and this very possibly was the forerunner of the malignant neoplasm. It seems logical to assume that the chronic gastritis was due to the continued

The tumor was described as polypoid and encircled approximately three fourths of the circumference of the stoma, its widest portion being near the side of the greater curvature. Microscopically it proved to be a carcinoma of multicentric origin, developing on the basis of multiple benign gastric polyps.

Singer stated that first a chronic gastritis had been initiated because of the irritation of the gastric mucosa by the intestinal secretions. This chronic gastritis was most severe in the neighborhood of the stoma. Multiple benign polyps then developed as the result of this inflammatory hyperplasia, and certain of these polyps ultimately underwent malignant degeneration. In this case there is convincing histologic evidence of the transition from inflammatory hyperplasia through benign to malignant neoplasia, and the gastro-enterostomy was, in all probability an important etiologic factor in the development of the carcinoma.

Singer also referred to three similar cases in the literature: the case of Schwarz,<sup>6</sup> the one of Hurst and Stewart<sup>7</sup> and the one of Eichelter.<sup>8</sup> These reports have been verified by me, and one possible additional case has been noted.

In the case reported by Schwarz a patient who had had an anterior gastro-enterostomy for a pyloric ulcer was relieved from symptoms for about six years, after which vomiting and loss of weight occurred. A laparotomy showed a carcinoma of the gastro-enterostomy stoma producing great dilatation of the proximal jejunal loop, while the distal loop was collapsed. There were metastases in the regional lymph glands and on the peritoneum. A Braun anastomosis was performed, and rapid recovery followed.

Hurst and Stewart made reference to a carcinoma of the gastro-jejunal ring, but clinical notes and a detailed description of the tumor are lacking.

A man of 59 was operated on by Eichelter for general peritonitis. Three and one-half years before, he had had a partial gastrectomy for a penetrating ulcer. At the time of his operation, Eichelter found a nodular tumor at the site of the anastomosis, and there was great dilatation of the proximal loop with perforation of an acute ulcer of the duodenum. A duodenojejunostomy with jejunostomy was performed. Death occurred two days later. Necropsy disclosed a firm growth, which originated at the anastomosis and encroached on the

6 Schwarz in discussion on Lengemann. *Operationsbefunde an Gastro-enterostomierten*, Zentralbl f Chir **53** 3000 (Nov. 20) 1926.

7 Hurst A. F., and Stewart M. I. *Gastric and Duodenal Ulcer*, New York: Oxford University Press, 1929, p. 429.

8 Eichelter G. Spontanperforation des paralytisch erweiterten Duodenalschenkels 4 Jahre nach subtotaler Magenresektion wegen ulcus (Primäres Karzinom an der Anastomosenstelle). *Deutsche Ztschr f Chir* **222** 106 1930.



# CHRONIC SUBDURAL HEMATOMA

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The study of chronic subdural hematoma may be divided chronologically into very definite periods. Prior to 1857 there were scattered records of observed cases of patients who were found at autopsy to have a collection of blood beneath the dura. In 1857 Virchow,<sup>1</sup> as a result of postmortem studies in a number of cases, introduced the term *pachymeningitis haemorrhagica interna*. Since in the cases studied by him there was no history of trauma he thought that the underlying pathologic process was the organization of an inflammatory exudate. From 1857 until 1925 the lesion was studied extensively by many pathologists and neurologists but with a few exceptions their chief interest was the underlying pathologic process rather than the treatment of the condition. A notable exception was an article by Trotter<sup>2</sup> published in 1914, in it four cases in which the condition was treated surgically were reported. Although very little of practical value has been added since, Trotter's contribution was generally overlooked until, in 1925, an excellent review of the literature and a report on twelve patients treated surgically was presented by Putnam and Cushing<sup>3</sup> in collaboration with other members of the Society of Neurological Surgeons. Of the twelve patients reported on eight recovered after operation for removal of the clot. This extremely valuable communication not only served to bring about a great revival of interest in a condition which is amenable to proper surgical treatment but also clarified to a great extent the confusion which had existed from the standpoint of the underlying pathologic process.

Putnam concluded that there were, in general two classes of hemorrhagic subdural hematoma. The first he called the vascular type and this is the lesion seen fairly frequently at autopsy on patients who have died of chronic alcoholism and of chronic wasting diseases. The histologic

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1 Virchow, R. *Haematoma Durae Matris*, Verhandl. d. phys.-med. Gesellsch. 7: 134, 1857.

2 Trotter, Wilfred. *Subdural Hemorrhage of Traumatic Origin and Its Relation to Pachymeningitis Hemorrhagica Interna*, Brit. J. Surg. 2: 271, 1914.

3 Putnam, Tracy J., and Cushing, Harvey. *Chronic Subdural Hematoma*, Arch. Surg. 11: 329 (Sept.) 1925.

*Examination*—The positive physical findings were (1) poor nutrition, (2) dental caries with many missing teeth, and (3) moderate tenderness without muscle spasm in the right lower and the right upper quadrant

The Kahn reaction of the blood was negative. Examination of the blood revealed a hemoglobin content of 80 per cent (Sahli) and a leukocyte count of 11,400. The urine was normal.

Roentgen studies on Aug 8, 1927, showed (1) "a normal stomach and duodenum, and (2) nonvisualization of the gallbladder by the Graham test." On Aug 13, 1927, roentgenograms showed a healthy chest. A tentative diagnosis of chronic cholecystitis was made, and it was thought that the symptoms were sufficiently severe to warrant operation.

*Operation*—Operation was performed on Oct 8, 1927, by Dr Hugh Cabot. Ethylene and ether anesthesia was used. The gallbladder was found to be normal.



Fig 1—Roentgenogram made on May 21, 1934, showing marked gastric retention and a filling defect in the lower portion of the stomach.

in all respects. The pylorus was involved in what appeared to be a chronic ulcer. This was dealt with by dividing the stomach just above the pylorus, thus disconnecting it from the duodenum. An end-to-side anastomosis was then performed between the stomach and the jejunum, a procedure which was thought to be a more satisfactory operation in this case than the usual posterior gastro-enterostomy, as the duodenum was still open. Before the end of the distal segment was closed, the noncrushing clamp was relaxed and the areas were examined, and the lesion was found to be entirely in the duodenum.

*Postoperative Course*—The convalescence was uneventful. The result of a check-up roentgen examination made on Oct 19, 1927, was reported as follows: "Postoperative examination of the upper part of the gastro-intestinal tract demonstrated the gastrojejunostomy stoma to be open and functioning well." The patient was discharged on Oct 22, 1927, on a Mills IV diet.

The most common factor occurring in the histories of patients with subdural hematoma is trauma. Not infrequently it is so trivial and occurs such a long time before that information in regard to it is not volunteered but has to be sought. This brings up the question of the mechanism by which these patients remain symptom-free for varying periods. This lapse of time between the trauma and the onset of symptoms has been called the latent interval. Recently it has been the subject of much speculation and some experimentation.

Trotter<sup>2</sup> concluded that the source of the hemorrhage was almost always one of the bridging veins running from the cortex across the subdural space into the superior longitudinal sinus. He thought that repeated small hemorrhages gradually increased the size of the hematoma until finally the limits of cerebral compression were reached. Putnam and Cushing<sup>3</sup> expressed the belief that this must be the correct explanation, and Keegan<sup>5</sup> cited as evidence of its truth a case in which at operation he found a small tear in the longitudinal sinus, from which there was bleeding only when the patient strained. From this he concluded that renewed bleeding was brought about by transitory rises in intracranial pressure. Leary<sup>6</sup> made postmortem studies on fifty patients with subdural hemorrhage and concluded that this explanation was correct.

Nevertheless, the theory has not been universally accepted, for in order to accept it one must conclude that bleeding into the subdural space violates practically all the rules for bleeding into the other tissue spaces of the body. Experimental investigation of the problem has been practically impossible, for no one has successfully produced typical subdural hematoma in experimental animals. Spiller,<sup>8</sup> in 1899, succeeded in producing the typical membranes in dogs by hemorrhage from the superior longitudinal sinus, but there was not the fluid content that is seen in clinical cases.

McKenzie<sup>9</sup> suggested the possibility of an increase in size of the sac by a process of osmosis. Gardner,<sup>10</sup> in a recent article, said that the

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5 Keegan, J. J. Chronic Subdural Hematoma. Etiology and Treatment, *Arch Surg* **27** 629 (Oct.) 1933.

6 Leary, Timothy. Subdural Hemorrhages, *J. A. M. A.* **103** 897 (Sept. 22) 1934.

7 Putnam, T. J., and Putnam, I. K. The Experimental Study of Pachymeningitis Hemorrhagica, *J. Nerv. & Ment. Dis.* **65** 260, 1927.

8 Spiller, W. G., and McCarthy, D. J. A Case of Internal Hemorrhagic Pachymeningitis in a Child of Nine Years, with Changes in the Nerve Cells, *J. Nerv. & Ment. Dis.* **26** 677, 1899.

9 McKenzie, K. G. A Surgical and Clinical Study of Nine Cases of Chronic Subdural Hematoma, *Canad. M. A. J.* **26** 536, 1932.

10 Gardner, W. J. Traumatic Subdural Hematoma, *Arch. Neurol. & Psychiat.* **27** 847 (April) 1932.



Fig 3—Photomicrograph ( $\times 85$ ) of the gastric mucosa near the gastroenterostomy stoma. The mucosa is thickened by an increase in size and number of the epithelial cells and by the heavy infiltration by lymphocytes and plasma cells. There is a marked increase in the formation of mucin and hyperplasia of the intrinsic lymphoid tissue.

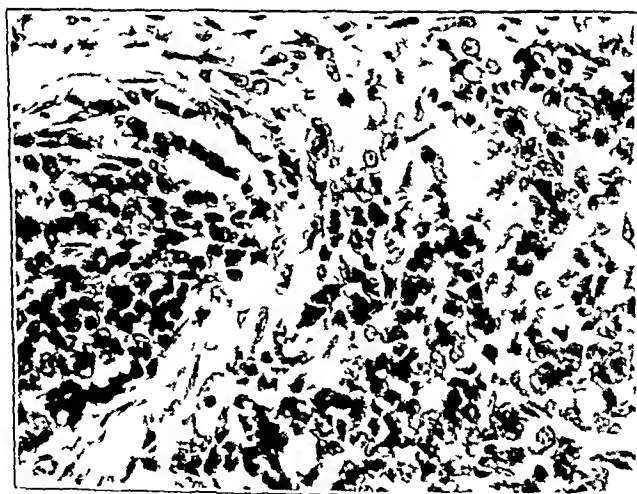


Fig 4—Photomicrograph ( $\times 400$ ) of the gastric wall near the gastroenterostomy stoma. Scirrhous carcinoma tissue infiltrates the muscle tissue and appears in the subserous connective tissue. Associated with the carcinoma is an active fibroblastic proliferation.

## REPORT OF CASES

CASE 1<sup>13</sup>.—J H A, a Negro aged 58, entered the Barnes Hospital on Nov 27, 1919. He was admitted to the medical service in a state of unconsciousness. Four months before he had been in an automobile accident and had been unconscious for twelve hours. What followed is not recorded, but a few days before admission to Barnes Hospital, he had been sent to a local hospital because of mental changes. He had been forgetful and irrational and had complained of dizziness. A lumbar puncture was made, after which he became much more stuporous, and the Cheyne-Stokes type of respiration developed. At the time of admission, he was unconscious and had bilateral choked disk, with hemorrhages in the right eye, pathologic toe signs on the left side and some spasticity of both arms. The left arm was not moved voluntarily.

A diagnosis of tumor of the frontal lobe on the right side, probably in the last stages of compression was made. With the concurrence of Dr Schwab the patient was transferred to the neurosurgical service, and because of his precarious condition a subtemporal decompression on the right side was decided on. The dura pulsated but had a bluish appearance, and when it was incised the membrane of a subdural hematoma was encountered. A large amount of old fluid blood was evacuated. As much of the membrane as could be reached was removed, and the wound was closed with silk.

Following operation the patient's state of unconsciousness became more profound. There was a rising blood pressure and a slowing pulse rate, hence the same night the wound was reopened. When the muscle sutures were removed, a large amount of old blood mixed with cerebrospinal fluid was evacuated. A rubber tissue drain was put in through the opened dura and the wound closed. The patient's condition gradually grew worse. He contracted pneumonia and died on November 30.

Autopsy was performed and such marked compression of the right hemisphere was present that the right ventricle was practically obliterated. There was a small amount of subdural hematoma on the left side, but no bleeding around the operative site. There was definite bronchial pneumonia.

*Comment*.—This case illustrates a number of important points. In spite of the definite history of trauma subdural hematoma as a diagnosis was not considered. There was marked aggravation of symptoms after lumbar puncture and the puncture was undoubtedly a great factor in the cause of death. Although the apparently correct treatment was carried out the patient did not improve after operation. In the discussion of the case by Putnam and Cushing<sup>13</sup> it was said that in spite of the decompression the edema of the brain progressed to such an extent that the ventricle was almost obliterated by swelling. This is an erroneous conception. What actually happened is that when the hematoma was removed a large "dead space" was left. The ventricle on that side had been markedly compressed and after operation the brain failed to expand so that at autopsy the ventricle on that side was still compressed as it had been before operation. Just how to deal best with this dead space is still a problem for in one other case the findings were similar (case 12).

13 This case is included in the study by Putnam and Cushing<sup>13</sup> as case 6.

chemical trauma to which the gastric mucosa was subjected by reason of the constant reflux of alkaline intestinal secretions from the jejunum

In an organ such as the stomach in which malignant disease is prone to occur it does not seem unreasonable to suppose that in the course of this inflammatory process the cells had exceeded the bounds of normal and orderly growth and progressed to the stage of blastomatous proliferation

Of the late complications occurring at the stoma in cases of gastro-enterostomy performed for duodenal ulcer, an inflammatory lesion originating chiefly on the jejunal side of the anastomosis (jejunal ulcer) is the one most commonly encountered. Apparently, as a rule, the mucous membrane of the jejunum is more liable to injury as the result of the altered physiology and chemistry produced by the operation than is the lining membrane of the stomach. Moreover, the incidence of malignant degeneration in persons with jejunal ulcer is insignificant, in analogy with the well known rarity of carcinoma of the upper portions of the small bowel

In the case herein reported and in the small number of similar cases found in the literature a reversal of this more usual course of events apparently took place following the gastro-enterostomy. Thus the major inflammatory changes occurred in the stomach, and perhaps from this hyperplastic inflammatory process carcinoma subsequently developed at the gastrojejunal ring, and obstructive symptoms finally developed as the growth seriously compromised the opening

A point of some additional interest is the fact that just as in cases of carcinoma of the lower portions of the stomach the neoplasm is usually found to end abruptly at the pylorus and rarely invades the duodenum, so in this case of gastric cancer involving over one third of the stomach, the growth was limited entirely to the gastric side of the anastomosis. Although the lesion completely encircled the stoma, both grossly and microscopically, the jejunum was found to have successfully resisted invasion by cancer cells

CASE 4—D W, a white girl aged 17 referred by Dr Frank Harrison of Dallas and Dr H V Copeland, of Grand Prairie, Texas, was admitted to the Barnes Hospital on May 4, 1928. There was no definite history of injury. Five months prior to admission the patient had an attack of unconsciousness, lasting for about five minutes, with no convulsive movements. She had four attacks similar to the first at intervals of about a month, without residual symptoms until the last attack eight days prior to her admission, which was followed by extreme frontal headache, nausea and vomiting. Shortly before admission, she had noticed that her vision was becoming poor and that she did not see as well to the right side as to the left. A few days before admission, she had noticed double vision and an inability to control accurately the movements of her left arm and hand.

Neurologic examination showed bilateral choked disk, lateral nystagmus, marked ataxia of the left hand and questionable weakness of the abdominal reflex on the left. The visual fields were normal. It was felt that the most probable



Fig 1 (case 3)—The displacement of the ventricular system to the left side as a result of the subdural hematoma on the right side

diagnosis was a tumor of the posterior fossa, but since the symptoms were rather indefinite, injection of air was necessary.

On May 10 an incision was made over each occipital pole and both ventricles were found collapsed. Only a few cubic centimeters of fluid was obtained, and this was replaced with air. The plates showed no air in the ventricular system. Because of the smallness of the ventricles, it was very unlikely that there was a tumor of the posterior fossa, so because of the possibility of a frontal lesion on the right side a subtemporal decompression was made on the same side on May 16. When the bone was opened, the dura looked bluish and when the dura was opened, some clot and old liquid blood escaped. The opening in the dura was made as large as possible and the wound closed.

Following operation, the choked disks did not subside. The patient's symptoms improved very little, and on May 23 a frontal flap on the right side was reflected and a typical subdural hematoma, which in places seemed rather old was exposed and removed.

picture in the membrane according to Putnam varies from the traumatic type in the size and appearance of the new-formed vessels in the wall of the sac which underlies the dura. These vessels, except for size have the appearance of normal capillaries. They are frequently 40 microns or more in diameter.

The second type which he called reactive or traumatic, is the one which concerns the surgeon. The gross appearance may be practically identical with that of the foregoing type but the clinical behavior is very different. Putnam stated that hematomas of this type may be differentiated histologically from that of the first type but that the difference is so slight that the two may be easily confused. In the wall of the sac just beneath the dura are irregular blood-filled spaces lined with mesothelium. These are much larger than the giant capillaries and the spaces frequently become confluent with each other. They anastomose with the normal capillaries seen in the wall of the sac.

It is with this reactive or traumatic type of subdural hematoma that this paper deals. I propose to show that (1) The condition is more frequent than is commonly supposed, (2) proper treatment when the condition is recognized sufficiently early offers a good prognosis, (3) the symptomatology is vague and the history of trauma may be so slight as to be entirely overlooked. In addition the records of sixteen cases treated in this neurosurgical clinic will be given.

#### CLINICAL BEHAVIOR

Subdural hematoma may occur at any age and in either sex but it is more frequent in men because of their greater exposure to injury. After an injury which may be very trivial or relatively severe there is an interval which may vary from a few days to months or even a year or more in which the patient is practically symptom-free. He then begins to present evidences of chronic progressive increasing intracranial pressure and not infrequently the diagnosis of tumor of the brain is made. He may come to the surgeon while his general condition is still good but all too frequently he arrives in a profoundly unconscious state and in the last stages of cerebral compression. The usual points in the history are headache, vomiting, gradual diminution in visual acuity, diplopia, convulsions, mental disturbances, etc. No one factor is common to all cases and in spite of the fact that the location of the hematoma is fairly constant over the convex portion of the cerebral hemisphere the findings on neurologic examination are extremely variable and frequently so confusing that in order to make the diagnosis it is necessary to resort to ventriculography<sup>4</sup> or to make trephine openings.

<sup>4</sup> Dandy, Walter E. Ventriculography Following the Injection of Air into the Cerebral Ventricles. *Ann Surg* 68:5 1918.



The patient's postoperative course was complicated by a flare-up of the pulmonary tuberculosis and the development of an abscess in the lung. She was discharged on April 8 in fairly good condition.

She was readmitted to the medical service of the hospital on June 25 because of pulmonary tuberculosis. The sputum contained tubercle bacilli, and roentgen examination showed evidence of tuberculosis at that time, but the neurologic condition was good. The patient was discharged on August 7, not greatly improved.

*Comment*—Decompression was performed in this case because the condition of the patient did not justify a more formidable procedure. The results were good. Here again there was a great scarcity of localizing signs but paralysis of the oculomotor nerve has not been uncommon in this series. In this case evacuation of the contents of the sac through a small opening was all that was necessary.

CASE 6—M. G., a white woman aged 60, referred by Dr. Francis Camp, Springfield, Mo., was admitted to the Barnes Hospital on March 17, 1930. There was no history of preceding trauma. A week before admission the patient acquired a very severe headache accompanied by vomiting. She became unconscious and had several generalized convulsions, and at the time of her admission to the Barnes Hospital she had been unconscious for three days.

Neurologic examination showed a patient in profound coma. Her eyegrounds were normal. There was a scar of an old corneal ulcer on the left eye. There were no signs of meningeal involvement and no other neurologic abnormalities except bilateral Babinski and Oppenheim reflexes. The pulse rate was rather slow. Roentgenograms of her skull showed no abnormalities. It was felt that this probably was not a condition requiring surgical intervention and that such intervention would be unwise. She was transferred to the neuromedical service and gradually increasing hyperpyrexia developed. Unconsciousness persisted, and she died on March 22, 1930.

Autopsy was performed. Over the left cerebral hemisphere the dura was greenish blue, and a typical subdural hematoma was present. It extended over the entire cerebral hemisphere on the left side with the exception of the tip of the temporal lobe. No fracture could be made out. In addition, the patient had aspiration pneumonia.

*Comment*—Here again there was no history of trauma and as the eyegrounds were normal, an incorrect diagnosis was made. Ventriculography, or better still exploratory perforator openings, would have made a correct diagnosis possible. However, the condition of the patient was such that surgical intervention was not considered.

CASE 7—R. A., a white boy aged 10 years, was admitted to the Children's Hospital on Dec. 17, 1930. There was a definite history of injury a month before admission, when he fell off a hay stack and struck his head. There was no loss of consciousness. The next day he complained of headache, vomiting and double vision. However, his mother said that the child had complained of headache for several months before the fall and that she did not believe the fall had anything to do with the present condition. His headache and diplopia had increased and his vision was becoming impaired.

wall of the sac acts as a semipermeable membrane and that as the complex protein molecules of the blood disintegrate, fluid enters the sac, thus increasing the bulk of the lesion. He reported experimental evidence to support the theory, and Zollinger and Gross,<sup>11</sup> after observation on an intact membrane removed surgically, stated that this is true.

#### TREATMENT

Surgical intervention is the only treatment of any avail for subdural hematoma. In this clinic, the practice has been to make an osteoplastic flap and remove the liquefied portion of the clot and as much of the surrounding membrane as possible. However, Trotter<sup>2</sup> stated that mere evacuation through an opening in the temporal fossa would result in a cure. Recently, McKenzie<sup>9</sup> reached the conclusion that the osteoplastic flap is usually unnecessary and may be dangerous. He advocated removing the contents of the sac by suction through a small opening in the bone and subsequent drainage of the subdural space for forty-eight hours. Fleming and Jones<sup>12</sup> reported eight cases, with one death, in which two openings were made and the contents of the sac washed out. In their series of eight cases, the hematoma was bilateral in 50 per cent, so that they made bilateral openings for exploration in every case.

There have been two chief reasons why the method of osteoplastic flap has continued in use in this clinic. In the first place, drainage through a small opening has not always been successful (cases 4, 7 and 9), and secondly, it has been felt that it is wiser to remove the membrane. Horrax (quoted by McKenzie<sup>9</sup>) on one occasion reflected a flap three months after the contents of a hematoma had been sucked out and found that both the outer and the inner membrane had disappeared. However, one cannot be sure from this single observation that this is always the case.

It is certainly true that evacuation through small openings is a much less formidable procedure than the use of an osteoplastic flap. It is also true that the patient not infrequently comes in a state of coma (five of sixteen in the present series), and since of the six patients in this series who died, five were in coma, in the future the method of treatment may be modified by using small openings for the patients in a comatose state and a flap when the patient's condition is good.

The following cases will serve to emphasize the points of importance in the diagnosis and treatment of the condition.

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11 Zollinger, R., and Gross, R. E. Traumatic Subdural Hematoma. An Explanation of the Late Onset of Pressure Symptoms, *J A M A* **103** 245 (Jul. 28) 1934.

12 Fleming, H. W., and Jones, O. W. Chronic Subdural Hematoma, *Surg Gynec & Obst* **54** 81, 1932.

Because of the definite history of alcoholism, the diagnosis was rather obscure. However, it was felt that the most probable diagnosis was chronic alcoholism complicated by the fracture of the skull.

About thirty-six hours after admission the patient became comatose, the blood pressure suddenly rose to 210 and the respirations became very labored. Death ensued in a short time.

At autopsy several fractures were noted in the left temporoparietal region, with a large subdural hematoma over the entire right hemisphere. The other organs showed no changes.

*Comment*—In this case operation was never considered. The diagnosis was missed entirely in spite of the definite history of trauma, slightly increased spinal fluid pressure and yellow spinal fluid. Again there is established the fact that a chronic subdural hematoma frequently shows no localizing signs. Had exploratory perforator openings been made or ventriculography been performed soon after admission, the outcome might have been different. This case also serves to emphasize the point that the only treatment of any avail is surgical removal of the clot. Lumbar puncture not only brings about no improvement but may be dangerous.

CASE 9—H. R., a white man aged 65, referred by Dr. O. D. Stanley, of Decatur, Ill., was admitted to the Barnes Hospital on July 6, 1932. Three weeks before admission he was in an automobile accident. He was unconscious for several hours but was apparently normal and was attending to his usual duties at the end of five days. Five days prior to admission he became unconscious and was taken to a hospital in another city, where hemorrhages in the eyegrounds were discovered. After he recovered consciousness somewhat, he was unable to move his left arm. His pulse had been rather slow. There had been no vomiting. At the time of admission he was markedly stuporous. The left eyeground showed a typical choked disk with large hemorrhages while in the right eye the margins of the disk were blurred and the veins full but there were no hemorrhages. There was a flaccid type of paralysis of the left arm and pathologic toe signs in the left leg. The diagnosis was subdural hematoma on the right side.

The patient was markedly dehydrated, and his stupor progressed to coma. After fluid had been given intravenously and subcutaneously, a flap was reflected on the right side on July 7. A perforator opening was made first to see if the clot could be washed out, but this was impossible, so a flap was reflected. The subdural hematoma was removed and the wound closed in the usual way.

Shortly after operation, the patient would respond but would immediately lapse into a rather deep stupor. This condition gradually improved, and he seemed to be in fairly good condition until the fourth postoperative day, when he began to have convulsions on the left side. These convulsions continued throughout the next day and at that time he showed definite evidence of bronchial pneumonia. He was put in an oxygen tent but in spite of all treatment he grew steadily worse and died on the eighth postoperative day.

At autopsy there was a fracture of the posterior wall of the frontal sinus on the left side with an area of infection at the site of the fracture. From this area a sinus extended back along the left side of the falx and a short distance back it eroded through the falx and extended into a large abscess in the right frontal lobe. In addition, there was evidence of severe bronchial pneumonia.

CASE 2—J R, a white man aged 40, was admitted to the Barnes Hospital on April 7, 1924. There was no definite history of injury. For a month before admission he had had rather severe headache and intermittent diplopia. The diplopia at times was so pronounced that it was almost impossible for him to drive his car. For several days he had had difficulty in swallowing and a disturbance in speech, and recently there had been a drooping of the left eyelid. He was markedly emaciated, but careful search for tuberculosis revealed no focus. Neurologic examination showed bilateral choked disk, weakness on the left side of the face and pathologic toe signs on the right side.

The uncertainty of the localizing diagnosis made ventriculography necessary, and on April 23 ventriculography was attempted. There was a greenish membrane beneath the dura on the right side, and it was impossible to make an opening into the ventricle on that side. An opening was made on the left side, and about 12 cc of bloody fluid was removed and replaced with air. Plates showed no air in the ventricular system.

On April 25 a subtemporal decompression was done on the right side, and the typical greenish-blue membrane of a subdural hematoma was found and removed.

The postoperative course was uneventful. At the time of his discharge on May 3, the patient was in good condition.

*Comment*—It is interesting that in spite of recognizing the bluish-green color which is so typical of subdural hematoma, ventriculography was still considered necessary. This also shows that trauma may be so slight that it goes unnoticed.

CASE 3—C R, a white girl aged 4 years, referred by Dr Paul C Carson, of Wichita, Kan., was admitted to the Children's Hospital on March 20, 1927. There was a definite history of injury a year before admission but there was not complete loss of consciousness. The patient had complained at intervals of headaches, which had recently become much more severe, and projectile vomiting had developed. She did not see as well with the right eye as with the left, but she was too young to be given tests for visual fields or visual acuity. Her head had always been rather large, but since the injury it had increased in size and measured 52 cm. There were bilateral choked disk and prominent veins on the forehead. A roentgenogram showed marked evidence of increased intracranial pressure.

Because of the lack of localizing signs, a ventriculogram was made on March 23, 1927. The ventricular system was displaced to the left (fig 1). On March 26, 1927, a large flap on the right side was reflected, and a typical subdural hematoma was exposed. This extended from the frontal region to the posterior parietal region, and when it was incised about 100 cc of old blood escaped. As much of the membrane as possible was removed, and the wound was closed in the usual way.

The postoperative course was entirely uneventful. At the time of discharge, on April 29, the patient was in excellent condition, and the neurologic examination showed no abnormalities.

*Comment*—In spite of the huge hematoma, there were no localizing signs. This was the first case in which a flap was reflected, and the results were excellent. The patient was the youngest in the series.

In this case the diagnosis of subdural hematoma was made by the use of a small opening in the bone but no attempt was made to evacuate the contents of the sac through this opening

CASE 11—J G M, a white youth aged 21, referred by Dr A B Jones, of St Louis, was admitted to the Barnes Hospital on Feb 1 1933

There was a definite history of injury three months before admission. The patient was in an automobile accident and received a severe blow on the head, which resulted in unconsciousness and lacerations of the scalp. The lacerations of the scalp were sutured, and as the patient recovered consciousness shortly after, he was allowed to go home from the local hospital. Afterward he had infrequent headaches for two months. A month prior to admission the headaches became almost constant, and he noticed blurring of vision.

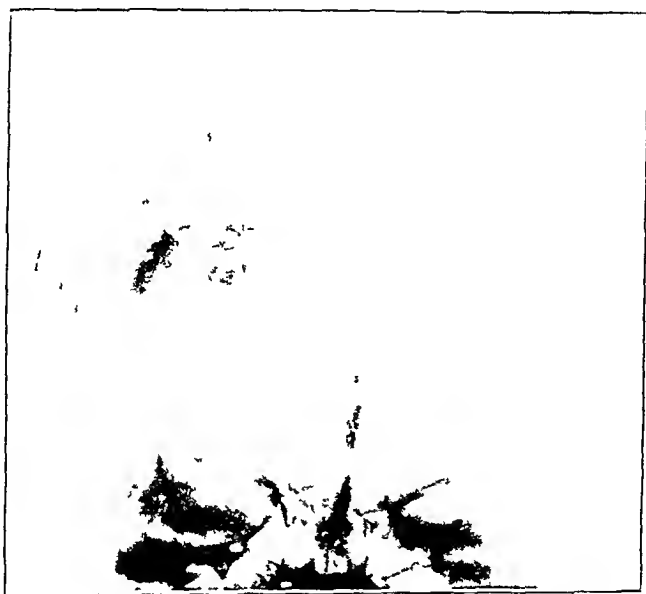


Fig 2 (case 11)—Normal ventricular configuration in spite of a large subdural hematoma on the right side

At the time of admission neurologic examination showed bilateral choked disks, facial weakness on the left side, central in type, an Oppenheim sign on the left and slight diminution in the abdominal reflex on the left. A calcified pineal gland was shown on roentgen examination, and this was displaced to the left of the midline. The preoperative diagnosis was a lesion in the right frontal lobe either subdural hematoma or tumor.

On February 6 a ventriculogram was made. About 8 cc of air was put into the left ventricle. Since this air would not go across into the right ventricle, air was put into the right ventricle. The plates looked normal (fig 2). In spite of the normal ventriculogram, however, a cerebral flap was reflected on the right side and a very large subdural hematoma was exposed and removed. A subtemporal decompression was left.

At the time of his discharge, the condition of the patient was excellent with the exception of choked disks, which were still present but were subsiding. He has been seen at intervals since his discharge and is normal in every respect.

The patient's postoperative course was uneventful. At the time of discharge, on the first of June, she was walking without difficulty. She has been perfectly well since.

*Comment*—Several interesting facts are illustrated by this case. There was again no history of injury. It is not at all unusual for this condition to be confused clinically with a lesion of the posterior fossa. Even in skilled hands ventriculography is not always easy or absolutely diagnostic. The results are interesting in connection with the recent controversy as to the best method of treatment. Putnam and Cushing<sup>3</sup> expressed the opinion that "on the whole a generous exposure of the lesion by osteoplastic resection with or without combined subtemporal decompression to accommodate the subsequent edema would seem to be the preferential method." Fleming and Jones<sup>10</sup> recently reported a series of eight cases in which the patient was treated by making anterior and posterior perforator openings and washing out the blood and clots contained in the sac. There was only one death in the series. McKenzie<sup>9</sup> felt that a large flap is usually unnecessary and may be dangerous. He added two cases to his original series, making a total of eleven cases. Of this number, five patients were operated on by the method of osteoplastic flaps with one death, and six had a small opening in the bone for drainage only. All six patients recovered. He stated the opinion that only one opening is necessary and that the subdural space should be drained for forty-eight hours. Rand<sup>11</sup> stated that the type of operation should be determined by the condition of the patient and that while he usually reflected a flap any procedure which evacuates the contents of the sac will give good results. The case just reported may be similar to that reported by McKenzie<sup>9</sup> as an instance of reformation of a hematoma, probably from postoperative oozing.

**CASE 5**—W. M., a Negress aged 24, was admitted to the Barnes Hospital on Feb. 6, 1930. Nine days before admission, during a period of intoxication, the patient was struck on the head with a lead pipe. She was unconscious for from ten to fifteen minutes. Since that time she had had headaches, and double vision had developed. At the time of admission she was somewhat stuporous, and her memory was very poor. There were numerous rales in her chest, and roentgen examination showed pulmonary tuberculosis.

Neurologic examination revealed little except complete paralysis of the third nerve on the right side. The eyegrounds were practically normal. The pulse rate was around 50 and the respiratory rate 12.

On February 10, because of increasing stupor, a subtemporal decompression was done on the right side. The dura was very tense and bluish, and when it was opened about 4 ounces (120 cc.) of old blood escaped. The cortex was markedly collapsed. A drain was put in, and the wound was closed.

<sup>14</sup> Rand, C. W. Chronic Subdural Hematoma, *Arch Surg* **14** 1136 (June) 1927.

was some extradural clot, but not enough to account for the symptoms. The patient also had well developed bronchial pneumonia.

*Comment*—This case illustrates the fact that psychotic symptoms are frequent and may be severe. The history was rather confusing, for some of the patient's associates stated that he had acted rather peculiarly before the accident, and there was also a suspicion that he had become addicted to some drug.

Much thought has been given to the part that the paraldehyde played. It was given in the usual dose, but after sleep was induced the patient could not be aroused, and his coma was so deep that no anesthesia was needed for the operation.



Fig. 3 (case 12)—Displacement of the entire ventricular system to the right side by the subdural hematoma on the left side.

The lumbar puncture has also been considered, but since it was done very cautiously, with the removal of only a few drops of fluid, it probably had nothing to do with the outcome.

**CASE 13**—A H, a white woman aged 47, referred by Dr. Charles Duden, of St. Louis, was admitted to the Barnes Hospital on June 10, 1933. She came in almost immediately following a fall down a flight of six steps. Immediately after the injury, she was not unconscious but soon became somewhat stuporous, and at the time of admission, although easily aroused, she would drop off to sleep if left alone. The only neurologic signs were a Babinski sign on the right and an Oppenheim sign on the left. A roentgenogram showed a fracture in the right parieto-occipital region, with no depression.

Neurologic examination showed bilateral choked disks with hemorrhage, weakness of the left sixth nerve, facial weakness on the right side, weakness of the right hand, hypo-active deep reflexes, an Oppenheim sign on the right and nystagmus, more to the right than to the left. A roentgenogram showed a pressure skull. The preoperative diagnosis was cerebellar tumor, but because of the scarcity of definitely localizing signs, it was thought that it would be wise either to give an injection of air or to make a ventricular estimation.

On December 22 openings were made over the occipital poles for injection of air, and when the dura on the left side was opened, a typical subdural hematoma was exposed. A small amount of this was removed, and it was decided not to do anything further at that time.

The child's condition remained apparently the same after this procedure, and on December 30 his father took him out of the hospital under protest, in spite of the fact that the danger to the child's vision had been explained to him.

On Feb 26, 1931, he was readmitted. At that time he still had bilateral choked disk and nystagmus. The abdominal reflex on the right was less active than that on the left.

On March 5, 1931, ventricular injection of air was made through the opening that had been previously made on the right side. The plates showed that the ventricular system was pushed over to the right side, so a flap was reflected on the left side. A typical subdural hematoma was exposed. When it was incised a large amount of old blood escaped, and the membrane was then stripped from the cortex. The wound was closed with silk in the usual way.

The postoperative course was uneventful, with the exception of slight trouble with fluid under the flap. At the time of his discharge, on March 15, the patient was in very good condition.

*Comment*—This is another example of the excellent results obtained in a child and again the question of small openings versus a large flap is raised. From the operative note it seems that there was certainly not complete evacuation of the contents of the sac through the small opening, and this may easily explain the lack of improvement.

CASE 8—M. R. V., a white man aged 45, referred by Dr. George B. Fletcher, Hot Springs, Ark., was admitted to the Barnes Hospital on April 5, 1932. This patient had been a moderate drinker of alcoholic liquors up to the year before admission, but during the past year he had been a sporadic dipsomaniac. For about ten months the patient's wife felt that he had been more irritable than usual, and on several occasions he had threatened suicide. Nine days before admission he went on one of his periodic sprees, and that evening he was found unconscious on the floor of his hotel room. During the next few days he was stuporous most of the time and complained of severe headache.

At the time of admission, he was stuporous but could be aroused. His memory was very poor, and he was disoriented. There was some tenderness in the left parietal region. His eyegrounds were normal. There was a questionable weakness on the right side of the face, and bilateral pathologic toe signs. The spinal fluid was yellow, and the pressure was 160 mm. of water. There were 90 cells without acetic acid and 45 cells with acetic acid. Roentgen studies showed a linear fracture in the parietal region with no depression. Wassermann tests on the blood and spinal fluid gave negative results.



*Comment*—This case again illustrates (a) the ease with which the causative trauma may be overlooked, and (b) the scarcity of localizing signs. In retrospect, one wonders if a less formidable operation might have influenced the result.

CASE 15—R. A., a white boy aged 15, referred by Dr. H. A. Kuhn and Dr. Ray Elledge, of Hammond, Ind., was admitted to the Barnes Hospital on Feb. 20, 1934. Three years before admission he was hit by a baseball bat in the temporal region on the left side. He had apparently been perfectly well until five months before admission, when he began to complain of occasional headache. These headaches persisted until a month before admission, when diplopia developed, followed shortly by complete paralysis of the third nerve on the left side. About a month before admission he began to have nausea and vomiting, and this had persisted at intervals until the time of his admission to the hospital. Two weeks before admission he had an attack of unconsciousness, without a convulsion, which lasted for several hours.

Neurologic examination showed paralysis of the third nerve and facial weakness on the right side, an Oppenheim sign on each side and a tendency to stagger to the right when walking. His eyegrounds were normal.

On February 24 a ventricular injection of air was given. The roentgenograms showed the ventricular system pushed over to the right, so a flap was reflected on the left side. The dura had the typical greenish-blue appearance of a subdural hematoma. The subdural hematoma covered part of the temporal lobe, a portion of the occipital lobe and all of the parietal lobe. A large amount of old bloody fluid, of chocolate color, escaped during operation. All of the membrane was removed and the wound closed in the usual way.

Following operation, the patient was totally aphasic, and the next morning he had a convulsion, which started in the right side of his face and became general. Following the convulsion he became extremely restless, so the flap was reopened. A fairly large clot between the bone and the dura was removed, but there was no evidence of subdural bleeding.

His general condition improved. He was totally aphasic for three days, when his speech gradually began to return. He was discharged on March 8. At that time the paralysis of the third nerve on the left side was still practically complete, and pathologic toe signs were still present, but the facial paralysis and aphasia had entirely cleared up.

*Comment*—If the history was correct this patient had a latent interval of three years. In the series of sixteen cases the shortest latent interval was six days and the longest three years. If the increase in size of a hematoma is due to repeated hemorrhages as has been stated by Trotter,<sup>2</sup> Putnam and Cushing,<sup>3</sup> Keegan<sup>4</sup> and others, there must have been some unusual factor in this case which brought about a renewed hemorrhage after a long interval of latency. On the other hand, one finds it extremely difficult to believe that it would take almost three years for the protein molecules of the blood in the sac to break down and osmosis to begin, as suggested by Gardner<sup>10</sup> and Zollinger and Gross.<sup>11</sup>

It is also difficult to explain paralysis of the third nerve on the right side with a subdural hematoma on the left. In this series, involvement

*Comment*—This case illustrates forcibly that an apparently mild injury to the head may have serious complications. Since in the cases that have been cited prior to this one there were few localizing signs it may be assumed that this patient's symptoms were due more to the abscess than to the hematoma. In reviewing the case, one might assume that his failure to improve should have suggested ventriculography or reexploration. However, a man of 65 who was at the point of death on admission was not a good subject for surgical treatment, consequently to do as little as possible was considered the wise policy.

In this case also an attempt to utilize a small opening in the bone was unsuccessful.

CASE 10—S. M., a white man aged 65, referred by Dr. Charles Compton, of Springfield, Ill., was admitted to the Barnes Hospital on Nov. 1, 1932. Two months before admission the patient, who was sheriff of his county, was struck during a fight. He fell and hit his head on the concrete walk and sustained a fractured skull. He remained in a hospital in another city in a semiconscious state for about a week. At the end of the week, lumbar punctures and hypertonic solutions resulted in some temporary improvement, but he soon became irrational and very difficult to manage. Two weeks before admission to Barnes Hospital, he left the local hospital and was taken home. While at home he had rather marked mental symptoms with delusions of persecution, and he refused to eat. There had been a few times when the patient seemed fairly alert mentally, but the family became alarmed because of marked loss of weight and he was brought to Barnes Hospital. A diagnosis of posttraumatic psychosis was made, and he was transferred to the service of Dr. A. D. Carr.

On November 4, the patient had a focal convulsion involving the right side of the face and the right arm and leg. However, it was not believed that his condition required surgical treatment. He remained in the hospital with periods of complete irrationality alternating with periods when he was fairly alert mentally until the latter part of January. At that time he was definitely going downhill, so it was decided to perform an exploratory operation.

A perforator opening was made over the right frontal lobe, and a subdural hematoma was immediately seen. A moderate-sized flap was reflected, and it was then seen that the hematoma was very small, covering only the surface of the frontal lobe. There were numerous adhesions between the cortex and the dura, and the cortex was yellowish in several places. The small subdural hematoma was completely removed.

Following operation, the patient improved rather remarkably and was discharged on March 7. At that time he was still having periods of slight mental confusion, but for the most part he was well oriented and seemed to be in excellent condition.

*Comment*—This case is an excellent example of a fact emphasized by Fleming and Jones,<sup>12</sup> i. e., that this condition may easily be mistaken for a posttraumatic psychosis. The convulsion occurred on the same side as the hematoma. It is still difficult to believe that this small lesion was responsible for all of the symptoms, but the fact remains that there was marked improvement after operation.

The patient's postoperative course was considerably prolonged because of repeated accumulations of fluid under the flap. He was discharged on August 21. At that time he was normal in every way except that the choked disks had not completely subsided.

In October 1934, the patient had a very severe seborrheic dermatitis around the incision. There was marked cutaneous irritation with some drainage for about two months. Roentgen examination at that time showed a possible slight area of osteomyelitis along the edge of the bone flap. On December 1 a portion of the incision was opened and a small bit of bone was removed. One or two silk sutures were also removed from the wound, and it was allowed to granulate in slowly. He was discharged from the hospital on December 29, and in a letter a month later he said that his scalp had entirely healed and that his condition was excellent.

*Comment*—In spite of a definite history of injury three months before, the presence of neurologic signs that are usually seen with a cerebellar lesion made it necessary to give an injection of air. The convalescence in this case was greatly prolonged as a result of accumulations of fluid under the flap, and the prevention of this has been one of the arguments advanced in favor of the small opening in the bone.

#### ANALYSIS OF SYMPTOMS

Since in cases of chronic subdural hematoma the symptomatology is extremely variable and frequently misleading an analysis of the prominent symptoms in this series of cases is of value (table 1).

TABLE 1—*Analysis of Symptoms*

	Forty-Two Cases (Jelsma)	Eleven Cases (McKenzie)	Seven Cases (Rand)	Sixteen Cases (Sachs and Furlow)
History of trauma	88%	91%	100%	86%
Male	93%	82%	100%	68 75%
Female	7%	18%	0%	31 25%
Headache	79%	100%	86%	88%
Choked disks	40%	91%	71%	68 76%
Reflex changes	76%	86%	56%	62 56%
Mental changes	86%	18%	56%	50%
Drowsiness	79%	90%	56%	50%
Cranial nerve changes	47%	9%	56%	50%
Vomiting	29%	54%	42%	44%
Motor disturbances	70%	55%	28%	36%
Coma	57%	28%	56%	30%
Nystagmus	11%	0%	14%	18%

Jelsma<sup>10</sup> analyzed the symptoms in forty-two cases reported in the literature and two cases of his own. McKenzie<sup>9</sup> tabulated the symptoms in nine of his cases for comparison with those of Jelsma,<sup>10</sup> and for completeness the two cases subsequently added by him were included in the tabulation, as was an analysis of the seven cases reported by Rand.<sup>14</sup> Ages of patients are not included for the lesion may be present

<sup>16</sup> Jelsma, Franklin. Chronic Subdural Hematoma, Arch Surg **21** 128 (July) 1930.

*Comment*—This case is interesting in retrospect. In spite of the definite history of trauma, the possibility of tumor was considered strongly enough so that ventriculography was considered wise. The ventricular system was apparently normal in configuration, but it was impossible by rotation of the head to get the air to pass from the left into the right ventricle. Had the openings for ventriculography been made over the region of the anterior horns instead of over the posterior horns, ventriculography would not have been necessary.

This is also the first case of subdural hematoma in which it was possible to utilize the pineal shift described by Naffziger<sup>15</sup> and it is difficult to understand how although the pineal body was displaced the ventricular system was in the normal position.

This is the first case in this series in which accurate localizing diagnosis by neurologic examination was possible. The smooth convalescence with prompt and complete recovery shows the great advantage in being able to treat a patient fairly early in the course of the disease.

CASE 12—H. B. G., a dentist aged 54, was admitted to the Barnes Hospital on Feb. 22, 1933.

There was a definite history of injury six weeks before, when the patient slipped on the ice and struck his head. He was unconscious for a very short time. The next day he returned to his usual work and had no further symptoms except that he complained of headache and general weakness. About two weeks after the injury the headaches became much more severe and were accompanied at times by nausea and vomiting. He acquired rather marked mental symptoms, which had progressed. He slept a good part of the time and was much confused. Two days before admission to the hospital, he was seen by Dr. Ernest Sachs at home. At that time he was absolutely unmanageable and examination was out of the question. He was admitted to the hospital as a patient of Dr. A. D. Carr, and a careful lumbar puncture was made, which showed the pressure of the spinal fluid to be 400 mm and the cell count 3. He was given paraldehyde to quiet him and soon dropped into a deep stupor, from which he could not be aroused. He was transferred to the neurosurgical service in deep coma. His eyegrounds were practically normal. The preoperative diagnosis was either subdural hematoma or a tumor of the frontal lobe, and on February 24 a ventriculogram was made (fig. 3). The roentgenograms showed a frontoparietal lesion on the left side, so a flap was reflected on the left side. A rather large subdural hematoma was exposed, and about 150 cc of unclotted blood was removed together with as much of the membrane as possible. When the wound was perfectly dry it was closed in the usual way.

The immediate postoperative condition was rather precarious, but after transfusion the blood pressure rose. However, on the following day the temperature was elevated and he was slightly cyanotic. Hypertension became marked, the patient's condition rapidly grew worse and he died about forty-eight hours after operation.

Autopsy was performed and showed that the subdural hematoma had been completely removed. The cortex was still rather markedly compressed and there

<sup>15</sup> Naffziger, Howard. A Method for Localization of Brain Tumors. The Pineal Shift, Surg., Gynec. & Obst. 40: 481, 1925.

This striking fact is worthy of emphasis. When the diagnosis was made and operation performed before the onset of coma, there was a mortality rate of only 9 per cent, but if operation was delayed until after the onset of coma and symptoms of marked compression, the mortality rate was 100 per cent.

For purposes of comparison, mortality rates in other reported series of cases of chronic subdural hematoma are shown in table 3.

As a result of the facts brought out in this series of cases, it is felt that the following opinions and conclusions are justified.

Chronic subdural hematoma frequently produces very few localizing signs. The three most important points in diagnosis are (1) the history of injury, (2) headache and (3) choked disks. However, the condition may exist in the absence of any or all of these signs.

TABLE 3—*Mortality Rates in Cases of Chronic Subdural Hematoma*

Authors	Total Number of Cases	Mortality Percentage	Mortality After Operation Percentage
Trotter <sup>8</sup>	4	50	50
Putnam and Cushing <sup>2</sup>	12	33½	33½
Rand <sup>6</sup>	7	28	16½
McKenzie <sup>9</sup>	11	9	9
Fleming and Jones <sup>4</sup>	8	12	12
Jelsma <sup>10</sup> (42 cases from literature and 2 cases of his own)	44	43.2	19.3
Sachs and Furlow	16	37.5	28

Ventriculography or exploratory perforator openings are very often necessary to make the diagnosis.

The surgical treatment of chronic subdural hematoma offers a good prognosis. However, the prognosis is vastly better if the patient comes to the hospital before the development of symptoms of marked cerebral compression.

The question of the best method of surgical approach is not definitely settled. It is my opinion that if the general condition of the patient is good the reflection of an osteoplastic flap is the method of choice. If the patient is in coma, I propose to modify the treatment, using the method of washing out the contents of the sac through two openings, as suggested by Fleming and Jones <sup>10</sup>. I do not believe that one opening, as suggested by McKenzie <sup>9</sup> is always sufficient and in support of my belief I cite three cases (cases 4, 7 and 9) in which this method failed.

She was treated with hypertonic solutions and seemed to do extremely well until the sixth day, when she had several brief convulsive attacks characterized by drawing of her head and eyes to the left. She also had one generalized convulsion. The next day she had several brief convulsions and beginning choked disks were noted. A diagnosis of subdural hematoma was made. Since there were no localizing signs it was decided to make periotor openings over both frontal lobes and in this way to determine the site of the hematoma.

The periotor opening on the right side was made first, since this was the side of the fracture and the subdural hematoma could be seen. A small flap was reflected, and when the dura was opened about 90 cc of old blood escaped. The typical membrane of a subdural hematoma was removed and the wound closed in the usual way.

The patient's postoperative course was entirely uneventful and she was discharged at the end of the second postoperative week.

*Comment*—This is one of the rare cases in which the condition develops under one's eyes so to speak. The symptoms began so soon after injury that one is not sure whether it is properly called *chronic* subdural hematoma but the subdural membranes were well formed. The excellent results show the advantage of early recognition.

CASE 14—W. V. M., a white man aged 49, referred by Dr. R. M. Purdie, of Houston, Texas, was admitted to the Barnes Hospital on July 16, 1933. He was a farmer and gave no definite history of injury. His illness began about eighteen months before with headache and vomiting. This condition had become progressively worse and for the past two to three months there had been an increasing diminution in the acuity of vision. About a month before admission there was an unusually severe attack of headache and vomiting with questionable loss of consciousness. After this his memory became markedly impaired and an athetoid tremor of both upper extremities developed.

Neurologic examination showed a marked decrease in visual acuity with slight papilledema in both eyes, diminished hearing in both ears, athetoid movements of the upper extremities and hyperactive deep reflexes with pathologic toe signs on the left, but because of the scarcity of localizing signs ventriculography was necessary. The diagnosis was probable tumor of the frontal lobe.

The ventriculogram made on July 19 showed a displacement of the ventricular system to the left. A flap was reflected on the right side. A subdural hematoma about 1.5 cm in thickness, was exposed and removed. There was marked atrophy of the convolutions beneath the subdural hematoma. A small piece of this atrophied cortex was removed for section.

The patient talked very well and seemed entirely rational about six hours after the operation, but at the end of fifteen hours he began to be very drowsy and difficult to arouse. This was attributed to cerebral edema and he was treated with hypertonic solutions, with slight temporary improvement. The following day he took fluids and tried to talk. His temperature was rather markedly elevated, and on July 22 because of the possibility of a postoperative clot a portion of the wound was reopened, but no clot was found. The following day, the patient had well developed bronchial pneumonia, his condition grew steadily worse, and he died on the fourth postoperative day.

Autopsy was performed but no evidence of postoperative bleeding was noted in the cranial cavity. There was well developed bronchial pneumonia.

finding are of great importance in the general field of physiology as well as in the immediate experimental and clinical problems of glandular transplantation. In spite of this fact, a search of the literature fails to reveal further experimental study to corroborate or refute Halsted's conclusions.

As a preliminary to an experimental study to test this "law of deficiency," the protocols of Halsted's experiments, which are recorded in admirable detail, were carefully studied. It became apparent that the evidence, though suggestive, was not conclusive. The results of the experiments by no means uniformly supported the concept, nor were the experiments themselves drawn up in such a way as to put the hypothesis to a test. It was observed that in most of the experiments it was impossible to determine the extent of the parathyroid deficiency. In many of the experiments the degree of deficiency which had existed at the time the graft was placed was altered by the removal of additional parathyroid tissue a week or two later. In other experiments grafts were placed in dogs in which grafts had already been placed from one to two weeks previously, so that the degree of deficiency existing at the time the second graft was transplanted was indefinite, as it depended on the functional condition of the first graft. Moreover, in only three of Halsted's experiments were the results confirmed by microscopic study.

The following experiments were undertaken to determine the importance of the factor of deficiency on the immediate survival of glandular transplants. The parathyroid gland of the dog is well suited for such a study since there are four glandules with fairly constant anatomic distribution, i. e., two glandules associated with each lobe of the thyroid gland. The removal of all four glandules results in fatal tetany, while the removal of three is followed as a rule by mild transient tetany. One or two glandules can be excised without any physiologic embarrassment.<sup>3</sup>

#### METHOD

Autoplastic transplantation of the parathyroid gland was performed in a total of thirty-four dogs. Pentobarbital sodium (32 mg per kilogram of body weight) administered intraperitoneally was employed as the anesthetic, and careful aseptic technic was observed. Each graft consisted of a single intact parathyroid gland which was reimplanted within a few minutes of its removal between the fibers of the adjacent muscles in the neck, with a silk suture placed to mark the location. The state of parathyroid deficiency was varied so that in one series only the one gland which was transplanted was molested, while the other three were not disturbed. In another series two glands were removed, one of these was grafted and the other discarded, while the two remaining glands were left in situ. In a third series all four of the parathyroid glands were removed, one

<sup>3</sup> Morel, L. Les parathyroides, Paris, A. Hermann & fils, 1912

of the third nerve was noted in three cases. In two of these cases it was contralateral and in one homolateral.

CASE 16—L. B., a white man aged 28, referred by Dr. Charles O. Lane, of West Frankfort, Ill., was admitted to the neuromedical service of the Barnes Hospital on July 27, 1934.

Exactly three months before admission the patient had received a blow on the head which made him unconscious for a few minutes. There was apparently a complete recovery from this, and the patient soon resumed his normal activities. Two and one-half weeks before admission he noticed that his vision was rapidly failing and he had a very severe headache. He also had nausea and vomiting, and the headache, nausea and vomiting continued up until the time of admission. The headache had been so severe that he had been confined to his bed continuously, and his vision had rapidly diminished.



Fig. 4 (case 16)—Dislocation of the ventricular system to the left side and compression of the right ventricle as a result of the subdural hematoma on the right side.

Neurologic examination showed marked diminution in the acuity of vision, bilateral choked disk with many hemorrhages and much exudate, lateral nystagmus, most pronounced on looking to the left, slight incoordination of the left hand and hypo-active deep reflexes. Roentgenograms showed marked pressure skull with the dorsum slightly forward.

With the definite history of injury, subdural hematoma was considered to be the most likely diagnosis, but because of the signs indicating involvement of the cerebellum ventriculography was necessary. This was performed on July 30. The entire ventricular system was found pushed over to the left (fig. 4), so a large flap was reflected on the right side. An enormous subdural hematoma was exposed and removed. When the most medial portion of the sac was removed, the dura over the longitudinal sinus was stripped from the bone, there was considerable troublesome bleeding, but this was finally controlled with a piece of muscle.



being replaced as a graft. Thus the state of deficiency varied from 25 to 100 per cent at the time the graft was placed. When only one parathyroid gland was removed great care was taken to disturb the thyroid gland as little as possible so as not to interfere with the blood supply to the second parathyroid

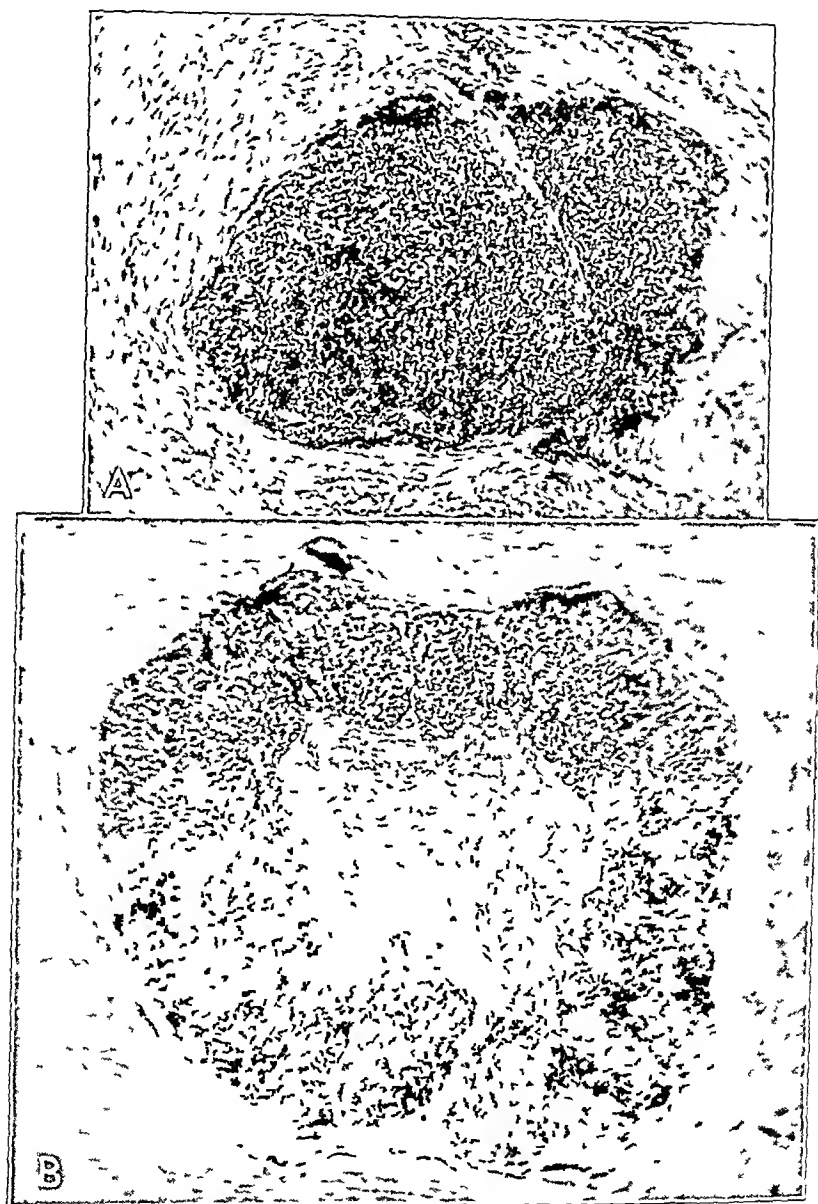


Fig 2—Sections of muscle containing grafts from dogs with a parathyroid deficiency of 50 per cent. The graft in *A* (dog C-164) was removed after forty five days, that in *B* (dog C-343) was removed after sixty-nine days.

gland on the same side. When two parathyroid glands were removed, this was accomplished by performing a thyroparathyroidectomy on one side, and when all four parathyroid glands were removed bilateral thyroparathyroidectomy was

at any age. In this series the youngest patient was 4 years of age and the oldest 65. Rand<sup>14</sup> reported one case in a man 90 years old.

As shown in table 1, the history of trauma is frequently obtained, and since trauma is the etiologic factor it is easy to understand why the lesion is so much more frequent in men than in women.

Headache is the most common complaint and choked disks the most common finding. Since the great majority of the cases analyzed by Jelsma<sup>16</sup> were reported by others, this might account for the low incidence of choked disks in his series. Pathologic reflexes are also common, but these reflex changes are frequently of no localizing value. In this series, ten patients had reflexes that were abnormal, and in five instances the pathologic reflexes were contralateral, in four cases bilateral, and in one homolateral.

Jelsma<sup>16</sup> emphasized the frequency of mental changes, while they were common, the incidence in this series was much lower than in his.

The frequency of occurrence of other signs may be seen in the table. An analysis will show merely that localization is frequently impossible by neurologic signs alone.

#### RESULTS AND CONCLUSIONS

Since this is one of the largest reported series of cases of chronic subdural hematoma from a single clinic, data on the final results are of value (table 2).

TABLE 2—*Analysis of Final Results in Sixteen Cases of Chronic Subdural Hematoma (Sachs and Furlow)*

Number of Cases	Number	Recoveries	Deaths	Mortality Rate Percentage
Total	16	10	6	37.5
Operated on	14	10	4	28.5
In comatose state	5	0	5	100
Conscious	11	10	1	9

There was a total of sixteen patients, and of these, six died, making a total mortality rate of 37.5 per cent. However, in two instances the condition was not correctly diagnosed, and operation was not performed. In each case the result was fatal. The operative mortality is based on four fatalities in fourteen cases, or 28.5 per cent. Further analysis shows that five patients were admitted in coma or became comatose soon after admission, and all died, giving a mortality rate of 100 per cent for comatose patients. There were eleven patients who were conscious. Of these patients only one died, giving a mortality rate of only 9 per cent in this group.



Figure 4, *A*, *B* and *C*

Fig 4—Sections of muscle containing grafts from dogs with a parathyroid deficiency of 100 per cent. The graft in *A* (dog C-382) was removed after fourteen days. *B* is the same section under high power magnification. The graft in *C* (dog C-9) was removed after twelve days, that in *D* (dog C-18), after twenty-three days (fatal tetany developing after removal and indicating that the graft had been physiologically active), and that in *E* (dog C-10), after twenty-nine days, showing follicular changes occasionally seen in transplants of parathyroid tissue.

# AUTOTRANSPLANTATION OF PARATHYROID GLAND IN THE DOG

AN EVALUATION OF HALSTED'S LAW OF DEFICIENCY

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The factors which determine the survival of glandular transplants have interested investigators and clinicians for years. It has been generally found that the transplantation of tissue into an individual of the same species—homografting—or into an individual of a different species—heterografting—is unsuccessful whereas the reimplantation of tissue into the same individual is frequently successful. Transplantation of the latter type, or autografting, is, however, not always successful. To explain the failures, it has been proposed that one of the important factors in determining the survival of autotransplants is the physiologic need of the organism for the tissue in question. Cristian<sup>1</sup> was the first to suggest such a deficiency as a determining factor, for he found that thyroid tissue engrafted into rats survived only after a partial thyroidectomy had been performed. His conclusion does not seem justified, however, since the tissue which was successfully transplanted was an autograft whereas that which was unsuccessfully transplanted, without partial thyroidectomy, was of necessity taken from another animal, and was therefore a homograft. Halsted<sup>2</sup> several years later arrived at a similar conclusion as a result of his experimental observations on autotransplantation of the parathyroid gland in dogs. He studied the effect of varying the degree of parathyroid deficiency on the viability of the transplant and concluded that the graft would not live unless a need for this graft had been created by excising more than one half of the previously existing parathyroid tissue. He found also that when two parathyroid glands were simultaneously transplanted under suitable conditions of deficiency, only one would survive. He therefore concluded that transplanted parathyroid tissue in excess of what is urgently required by the organism does not live. This concept has enjoyed wide recognition and indeed has frequently been referred to as "Halsted's law of deficiency." The teleologic implications of this

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From the Laboratory of Surgical Research, Harvard Medical School

1 Cristian, H. Evolution des greffes thyroïdiennes superflues, *Compt. rend. Soc. de biol.* **58** 361, 1905

2 Halsted, W. S. Auto- and Isotransplantation, in Dogs, of the Parathyroid Glandules, *J. Exper. Med.* **11** 175, 1909

several dogs by administering large doses of viosterol or parathyroid extract post-operatively—a possibility which comes to mind if the “law of deficiency” holds true. In three dogs in which a transplantation had been performed with a deficiency of only 25 per cent the functional as well as the microscopic survival of the graft was tested by removing the remaining three parathyroid glands at a second operation and observing the dog for tetany.



Fig 5—Section of muscle containing a graft from dog C-62, with parathyroid deficiency of 100 per cent. *A* shows the graft removed after sixty days. The dog had received 30 drops of viosterol daily since the time of grafting. *B* shows the same section under high power magnification.

After an interval varying from five to one hundred and thirty-four days the segment of muscle containing the graft was removed and examined microscopically.

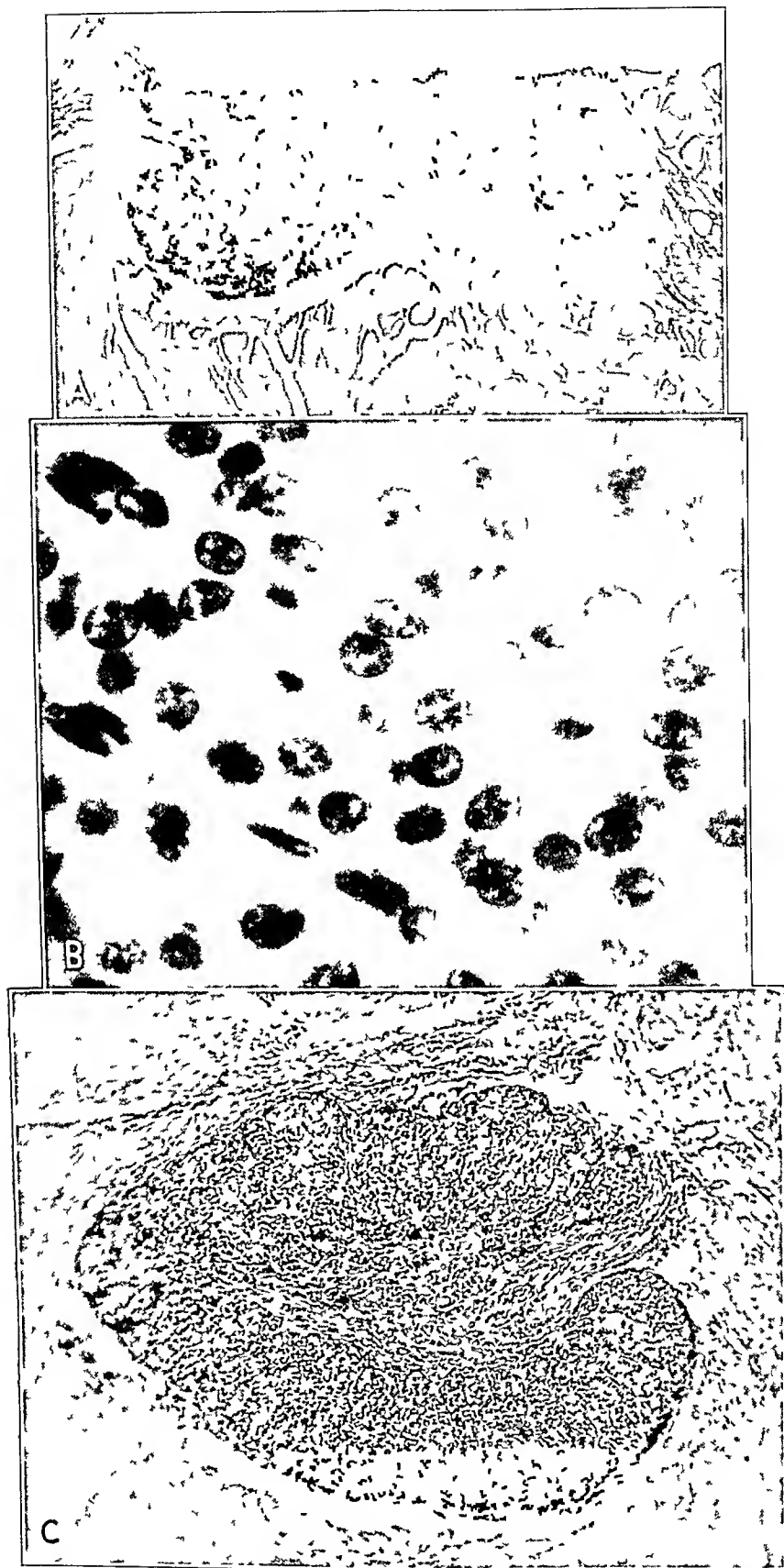


Fig 1—Sections of muscles containing grafts from dogs with a parathroid deficiency of 25 per cent *A* shows the section from dog C-11, from which one parathroid gland had been removed and reimplanted into the muscle of the neck. The graft was excised after twenty-one days *B* shows the same section under high power magnification *C* is the section from dog C-136. The graft was excised after twenty-eight days. Removal of the remaining three parathroid glands three days previously failed to cause tetany, indicating that the graft was functioning.

of the grafts showed partial replacement by fibrous tissue, and in a few of the experiments the graft could not be found. In these the graft may have been overlooked in sectioning the block of muscle or had perhaps been completely absorbed. These changes, however, were seen in the experiments in which the deficiency was 100 per cent about as frequently as in those in which it was only 25 per cent.



Figure 6, *A* and *B*

Fig 6—Sections of muscle containing grafts removed from dog C-103, with parathyroid deficiency of 100 per cent. Two grafts were placed simultaneously, one in either side of the neck. *A* shows the graft removed from the right side after sixty days, *B*, the same section under high power magnification. *C* shows the graft removed from the left side after sixty days, *D*, the same section under high power magnification.

The microscopic study of the grafts is interesting as regards the nature of the fibrotic changes. The fibrosis was never diffuse but was



Fig 3—Sections of muscle containing grafts from dog C-60 with a parathyroid deficiency of 50 per cent. Two grafts were placed simultaneously, one in each side of the neck. *A* shows a graft removed from the right side after sixty days. *B* shows the same section under high power magnification. *C* shows the graft removed from the left side after sixty days.



This study has not included the question of the survival of the grafts over a period of years. It is possible that the factor of deficiency may play a rôle in the ultimate survival of these grafts, although my experiments have shown nothing to indicate this.

#### CONCLUSIONS

1 Autotransplantation of the parathyroid gland in dogs is successful when only one parathyroid gland has been removed as well as when all four have been removed.

2 When two autografts are transplanted simultaneously they may both survive when the parathyroid deficiency at the time of grafting is only 50 per cent as well as when it is 100 per cent.

3 The administration of large amounts of parathormone or viosterol does not inhibit the survival of an autograft of parathyroid tissue.

4 The urgent physiologic need of the organism for parathyroid tissue does not appear to be a requisite for the survival of the autograft.

The photomicrographs were supplied by Dr. Robert Gross.

performed. Since a dog deprived of all four parathyroid glands will die of tetany within a few days unless proper measures are taken, the dogs in the latter group were prepared by giving them from 10 to 20 drops of viosterol daily for from two to three weeks before operation and calcium lactate by mouth for from one to two weeks postoperatively.<sup>4</sup>

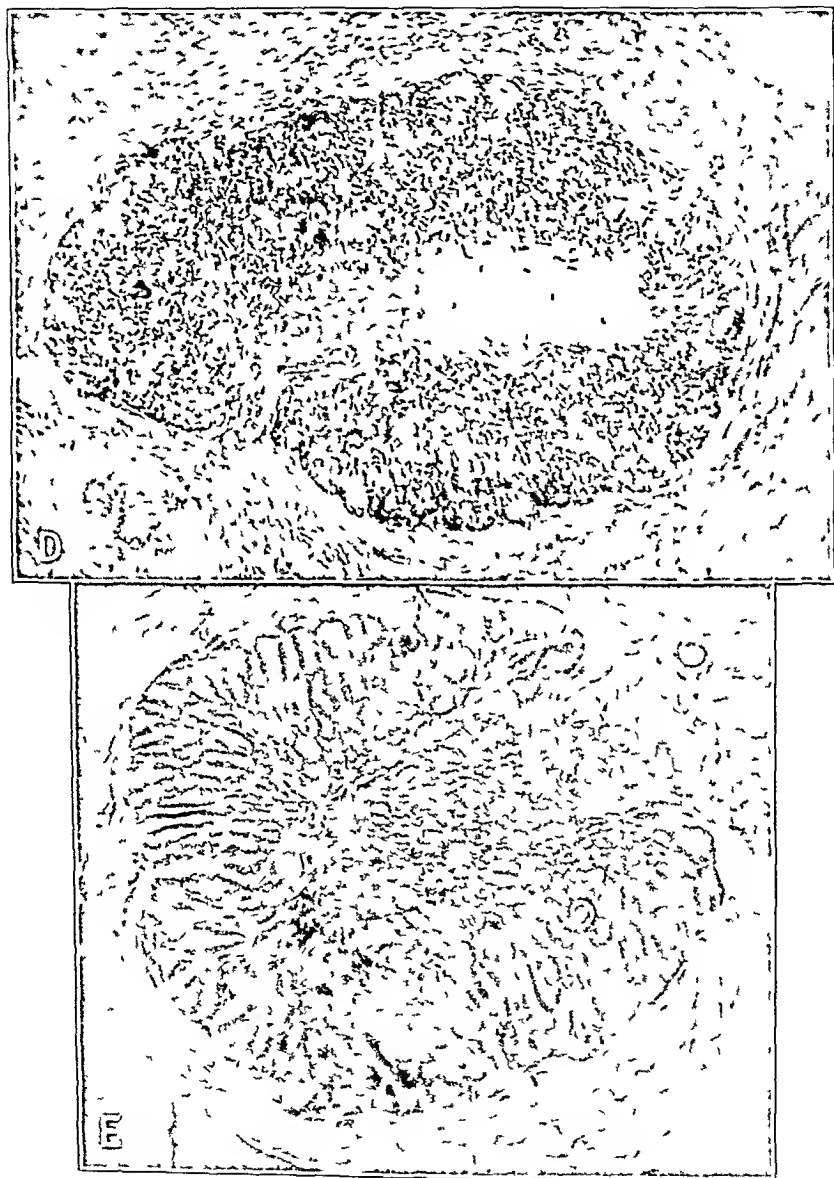


Figure 4, D and E

In several dogs two grafts were placed at the same time, one in the muscle on either side of the neck, to see whether, as Halsted had found only one of these would survive. An attempt was made to prevent the survival of the graft in

<sup>4</sup> Jones, J. H., Rapoport, M., and Hodes, H. L. The Effect of Irradiated Ergosterol on Thyroparathyroidectomized Dogs, *J. Biochem.* 86:267, 1930.

incisions in the upper part of the abdomen and especially frequent after operations on the gallbladder and gastro-enterostomies, and they expressed the belief that the major causes are cough, infection and gastric lavage. Their mortality rate was 44 per cent of all eviscerations.

Colp<sup>3</sup> expressed the belief that the underlying lesion is the important factor in evisceration.

Grace,<sup>4</sup> like Sokolov and Meleney and Howes, found the largest number of eviscerations after operations in the upper part of the abdomen. He found the mortality lower in those patients in whom evisceration occurred before the fifth day postoperatively than in those in whom it occurred later. White<sup>5</sup> agreed as to the frequency of evisceration following operations in the upper part of the abdomen.

Baldwin<sup>6</sup> noted that he had observed no evisceration since he began leaving sutures in place for fourteen days and keeping patients in the hospital for three weeks.

Von Gusnar<sup>7</sup> reported 10 cases, all in men, and listed the occurrence as 0.41 per cent of the laparotomies performed at his hospital.

Sigalas<sup>8</sup> published an excellent review of the literature and analyzed the 163 cases reported there plus 8 cases from his practice and that of his colleagues. He found that 127 of the patients were women, 30 were men and the sex of the remaining 14 had not been noted. He found, contrary to reports of the writers previously mentioned, that a larger number of cases were in patients with incisions in the lower part of the abdomen and that gynecological operations were the most common type. Freeman<sup>9</sup> also found that eviscerations occurred most commonly after operations on the lower part of the abdomen. Only 11 cases of carcinoma were listed by Sigalas. He expressed the belief that neither the type of suture nor the time of its removal is of any importance.

Starr and Nason<sup>10</sup> reported the results of a fifteen year survey, with 2,455 abdominal operations performed and 15 eviscerations, an incidence of 0.61 per cent. They agreed with Sigalas that eventration was most frequent after incisions in the lower part of the abdomen.

Some of the authors did not mention the number of cases on which their conclusions were based, others said nothing as to whether cases of gynecological and obstetric conditions were included in their study.

3 Colp, Ralph. *Ann Surg* **99** 14 (Jan) 1934.

4 Grace, R. V. *Ann Surg* **99** 28 (Jan) 1934.

5 White, W. C. *Ann Surg* **99** 34 (Jan) 1934.

6 Baldwin, J. F. *Am J Surg* **25** 7 (July) 1934.

7 von Gusnar, Kurt. *Arch f klin Chir* **150** 636, 1928.

8 Sigalas, M. *Rev de chir, Paris* **51** 32 (Jan) 1932.

9 Freeman, L. *Causes of Postoperative Rupture of Abdominal Incisions*,

*Arch Surg* **14** 600 (Feb) 1927.

10 Starr, A., and Nason, L. H. *Postoperative Rupture of Abdominal Wounds*, *J A M A* **100** 310 (Feb 4) 1933.

## RESULTS

*Parathyroid Deficiency of 25 per Cent, Single Graft*—Nine dogs were used. The graft could not be found in three, and the specimen was lost in one. Of the five grafts studied microscopically, all were living, three showing slight fibrosis and two marked fibrosis (fig. 1). The functional test was performed in three of these dogs by removing the remaining three glands at a second operation. Two of the dogs showed no tetany, indicating that the graft was functioning, and the third dog died of tetany. The specimen in this animal was lost.

*Parathyroid Deficiency of 50 per Cent, Single Graft*—Eight dogs were used. The graft could not be found in two. Of the six grafts studied microscopically, five were living, with moderate fibrosis (fig. 2), and one was necrotic, apparently resulting from a low grade infection.

*Parathyroid Deficiency of 50 per Cent, Two Grafts Placed*—One dog was used, a gland being implanted into the muscle on either side of the neck and examined microscopically two months later. Both grafts showed slight fibrosis and, as far as could be judged histologically, were functionally active (fig. 3).

*Parathyroid Deficiency of 100 per Cent, Single Graft*—Twelve dogs were used. The graft could not be found in two. Of the ten grafts studied microscopically, four showed slight fibrosis, four moderate fibrosis and two were necrotic (fig. 4).

One dog was given 1 cc. of parathyroid extract subcutaneously daily for one month following operation. At the end of this period the graft was in good condition with virtually no fibrosis.

One dog was given 40 drops of viosterol daily for two months postoperatively, as well as the usual preoperative preparation. At the end of this period the graft was in good condition, with very little fibrosis (fig. 5).

*Parathyroid Deficiency of 100 per Cent, Two Grafts*—Two dogs were used. All four grafts were recovered. In one dog they were living but showed moderate fibrosis at the end of one month. In the other dog both grafts were in excellent condition, with very little fibrosis, at the end of two months (fig. 6).

## COMMENT

In the foregoing studies it is seen that the graft survived and in many instances retained its original size and structure in experiments in which a deficiency of only 25 and 50 per cent had been created as well as in those in which there was a deficiency of 100 per cent. Most

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5 In determining the degree of parathyroid deficiency a possible source of error lies in the occasional occurrence of accessory parathyroid glands. These are said (Shapiro and Jaffe, *Endocrinology* 7:720, 1923) to occur in dogs with a frequency of about 6 per cent. Thus the exact degree of parathyroid deficiency in the individual experiments cannot be determined. However this factor must have been largely canceled by the number of dogs used in each of the foregoing series of experiments. Moreover, one can assume that functionally this accessory parathyroid tissue is of little physiologic importance during the first few days after operation or during the period in which the immediate survival of the transplant is at stake, because it is never sufficient to prevent fatal tetany in dogs deprived of all four parathyroid glands unless artificial substitution therapy is given.

# Essential Details of 32 Cases of Evisceration Following Abdominal Operation

Patient, Sex, Age	Diagnosis and Operation	Incision	Suture	Postoperative Course	Time of Evisceration (in Days Postop- eratively)	Result Other Condition
1 E A F 43	Adenocarcinoma of right ovary, panhysterectomy	Infra umbilical midline		Normal	13	Good
2 F A F 26	Pregnancy, cesarean section	Infra umbilical midline	Tension	Broncho pneumonia	9	Good
3 S A F 36	Fibromyoma, hysterectomy, salpingectomy	Infra umbilical midline	Tension	Gangrene of buttocks, had 7 high voltage roentgen treat- ments before operation	11	Good, arterio- sclerotic heart disease
4 A B M 17	Buerger's disease, ganglionectomy	Left para median	No tension	Coughing	6	Death, thrombi of superior mesenteric vessels
5 M B F 49	Fibromyoma, panhysterectomy	Infra umbilical midline	No tension	Normal	7	Good
6 F B F 49	Fibromyoma hysterectomy	Infra umbilical midline		Lavage, wound infection	9	Death
7 D C F 53	Carcinoma of descending colon, cecostomy	Right rectus		Lavage, pulse weak, wound infection	11	Death
8 L D M 52	Perforated duodenal ulcer, gastro enteros- tomy	Midline upper abdominal		Wound infection	13	Good
9 A D M 42	Intestinal obstruction, exploratory	Lower left rectus	Tension	Irrational	4	Death rupture of ileum
10 R F F 24	Chronic chole- cystitis, chole- cystectomy and appendectomy	Upper right rectus	Tension	Vomiting	8	Good
11 E F F 49	Fibromyoma panhysterectomy	Infra umbilical midline		Normal	6	Good
12 A F F 42	Fibromyoma panhysterectomy	Infra umbilical midline	Tension	Vomiting	4	Death rheumatic heart disease
13 H G M 38	Perforated gastric ulcer, suture of perforation	Epigastric midline	Tension	Coughing	9	Good
14 S G F 53	Fibromyoma panhysterectomy	Infra umbilical midline	Tension	Lavage	9	Good diabetes
15 S I F 65	Myofibro- sarcoma hysterectomy	Infra umbilical midline	No tension	Coughing	8	Good
16 B K F 42	Fibromyoma, hysterectomy	Infra umbilical midline	Tension	Vomiting	6	Good
17 S L M 40	Gastric carcinoma, resection	Epigastric		Coughing	14	Good
18 V M M 54	Cholecystitis with stones cholecystectomy appendectomy	Upper right rectus	Tension	Normal	8	Good
19 H M F 51	Fibromyoma, panhysterectomy	Infra umbilical midline	Tension	Normal	5	Good
20 M M F 30	Cesarean section	Infra umbilical midline	Tension	Coughing	6	Good

confined to the center and periphery of the transplants. This finding in itself might suggest that there was no general inhibitory endocrine factor involved. It seems likely that the central fibrosis which was as a rule more extensive in the larger grafts, represents the initial necrosis

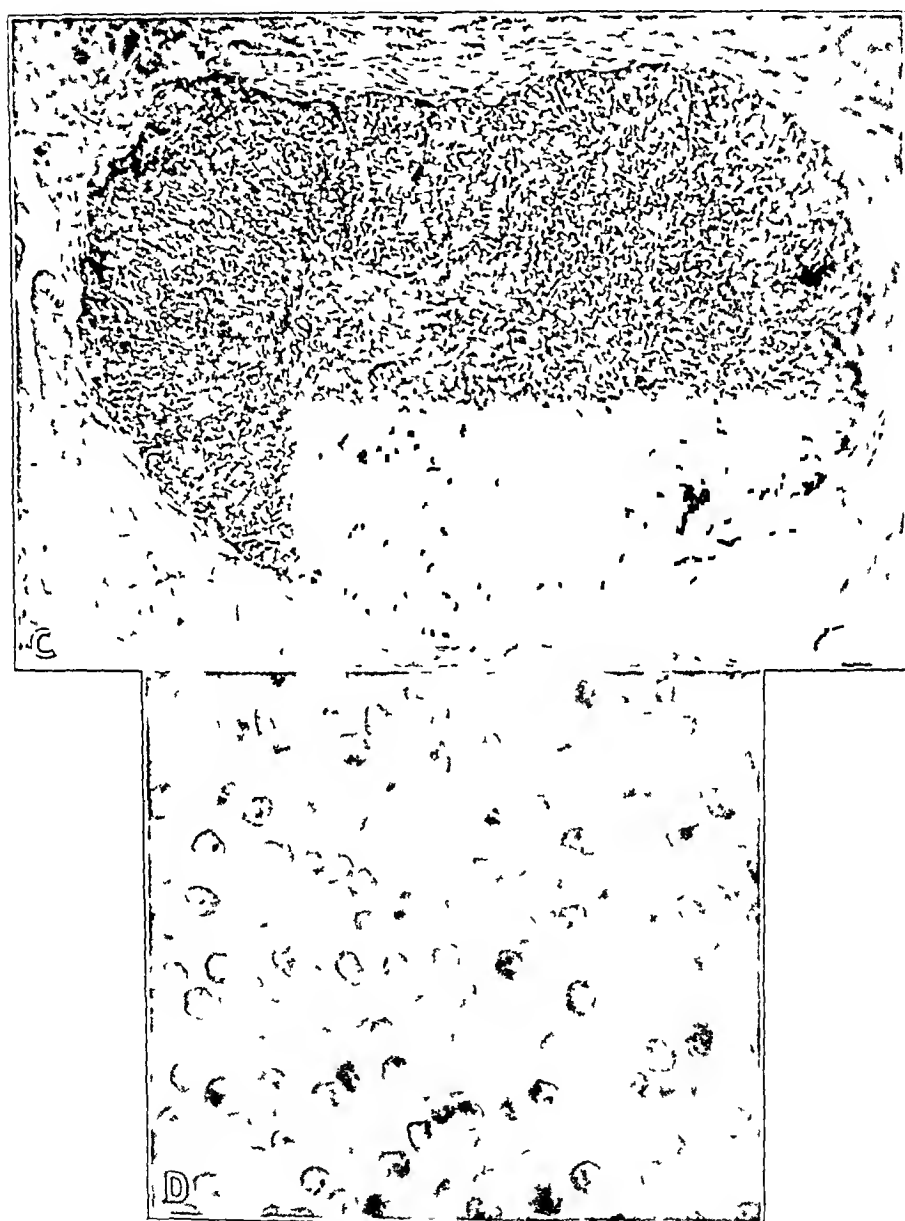


Figure 6, C and D

of that portion which was not revascularized sufficiently soon from the surrounding muscle. The peripheral fibrosis probably represents reaction to the trauma at the time of grafting. It did not appear to be progressive as it was not more marked in grafts of two or three months' duration than in those removed for study after only two or three weeks

evisceration occurred between two tension sutures while these sutures were still in place and intact as shown at the time of secondary closure

Most of the investigators cited who have made any note as to the most common period postoperatively in which evisceration occurs have found that in the majority of the cases the rupture occurred between the seventh and the tenth day. Of 31 cases in which we have a record of the time of the rupture evisceration occurred in 19, or 59.4 per cent between the sixth and the ninth day, with 6 cases each on the eighth

	OPERATIONS										PERCENT	
hysterectomy											40.6	13
gallbladder											9.4	3
											9.4	3
gastric resection											6.3	2
perf & ulcer											6.3	2
ganglionectomy											3.1	1
caesarian											9.4	3
laparotomies											6.3	2
cong. deform											3.1	1
l rectus											3.1	1
r rectus											3.1	1
carcinoma & sarcoma											18.8	6

	POST-OPERATIVE DAY											
4											3	
5											2	
6											5	
7											2	
8											6	
9											6	
10												
11											3	
12											1	
13											2	
14											1	

Chart 1—Incidence of evisceration according to type of operation and number of days after the operation

and the ninth day. Three patients had rupture of the abdominal wound as early as the fourth day and 1 as late as the fourteenth day. Of the 3 cases in which evisceration occurred on the fourth day 1 was an instance of hysterectomy in a patient with organic heart disease and mitral insufficiency, the second was one of exploratory laparotomy for suspected cholecystitis with an adherent inflamed and retrocecal appendix as the only finding, the third case was one of obstruction of the transverse and descending colon by large fecal masses. Of 7 cases in which evisceration occurred between the eleventh and the fourteenth

# EVisCERATION FOLLOWING ABDOMINAL OPERATIONS

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The occurrence of evisceration following laparotomy seems to be unpredictable. The uncertainty of this infrequent complication is its chief terror. We have made a survey of the cases occurring in Michael Reese Hospital during the past ten years and have analyzed those factors which seemed of importance to us, without however being able to reach any definite conclusions.

In going through the more recent literature on this subject, we found that Sokolov<sup>1</sup> had analyzed the largest series. He studied reports of 732 cases collected from clinics throughout Europe and even from America. Not all the case histories gave all the information he desired. He found that almost twice as many men were eviscerated as women and that the highest incidence (55.5 per cent) was in the first six months of the year, which he thought was due to a lowering of the vitamin C content of the body. He found that incisions in the upper part of the abdomen ruptured more frequently than did incisions in the lower part, that the greatest number of ruptures were in cases of malignant disease and that operations on the stomach headed the list of types of operations after which evisceration occurred. He stated that evisceration occurs after from 2 to 3 per cent of all laparotomies. He found that the maximum number of eviscerations occurred between the seventh and the tenth day postoperatively and that the largest number occurred in patients between the ages of 30 and 60. The mortality was 32.1 per cent in cases in which resuturing was done and 35.5 per cent in cases in which it was not done.

Meleney and Howes<sup>2</sup> in their study found that only from 1 to 2 per cent of the abdominal operations performed at the Presbyterian Hospital in New York were followed by evisceration. They agreed with Sokolov as to the postoperative period in which most ruptures occurred. Meleney and Howes found evisceration most common after vertical

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From the Gallbladder Group, Michael Reese Hospital.

1 Sokolov, S. S. Vestnik khir. 45-46:219, 1931, Internat. Abstr. Surg. 55:157, 1931, Ergebn. d. Chir. u. Orthop. 25:306, 1932.

2 Meleney, F. L., and Howes, E. L. Disruption of Abdominal Wounds with Protrusion of Viscera, Ann. Surg. 99:5 (Jan.) 1934.



three hours after a secondary closure had been done. Two had had hypertensive heart disease and arteriosclerosis. One of these patients died. The other had a hysterectomy for fibromyoma, but previous to her admission to this hospital she had had seven high voltage roentgen ray treatments over a period of two years, while she was in the hospital and on her fourth postoperative day, a gangrenous area developed over the buttocks, which was diagnosed as a roentgen ray burn, so we cannot but question whether these treatments affected the healing powers of the patient. One patient had thrombo-angitis obliterans with spasticity of the vessels of the leg. A ganglionectomy was done, with marked improvement in the efficiency of the circulation in the patient's legs, but evisceration occurred on the sixth day, and he died eleven days later. Postmortem examination showed arteriosclerotic stenosis and ulceration of both the mesenteric arteries and veins, with terminal thrombosis.

Twelve of our patients died. This mortality, 37.5 per cent, is in agreement with the figures given by other writers. All our patients had secondary closures. In view of Grace's statement that the mortality is lower in those cases in which evisceration occurs before the fifth day, we studied our cases from this point of view. Of the 5 patients in whom evisceration occurred on or before the fifth day, 4, or 80 per cent, died, all 3 of those in whom evisceration occurred on the fourth day died. Of the 26 patients in whom evisceration occurred after the fifth postoperative day, 8, or 31 per cent, died.

In the study of these 32 cases the one feature which struck us most forcibly was the fact that the incidence of evisceration was not spread evenly over the ten years but seemed to occur in groups, (this fact was noted by Maes and his associates<sup>12</sup> likewise) for example, from August 1925 until January 1929, there was but a single evisceration, and again during the period from March 1932 to January 1934 there were no eviscerations. On the other hand, there were 2 eviscerations in May 1925, 3 in July 1931, 5 from January to March 1932, 3 during September and October 1934. This grouping of eviscerations is not explicable on the basis of epidemics of grip, bronchopneumonia or other infections. No change in operating room technic can be held accountable. During the period from March 1932 to January 1934, during which not a single evisceration occurred, a certain brand of catgut was used exclusively, while a different brand of catgut was used during the preceding and subsequent periods, in which 5 eviscerations occurred in three months and 2 in one month. However, as there have been periods of several months without an evisceration even

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12 Maes, U., Boyce, F. F. and McFetridge, E. M. Post-Operative Evisceration with Analysis of Forty-Four Cases, *Ann Surg* 100:968 (Nov.) 1934.

In our own investigation we have included all cases of rupture of abdominal wounds with protrusion of the omentum or the viscera. We found 32 cases of evisceration occurring between Jan. 1, 1925, and Jan. 1, 1935. During this same period there were 12,445 abdominal operations, including 5,262 appendectomies. Most of these appendectomies were made with the McBurney incision, one which many authors feel is not conducive to evisceration. We think that it would, perhaps, make our percentage of incidence of evisceration more accurate if we subtracted most of the 5,000 appendectomies from our total number of laparotomies, leaving approximately 7,500 operations exclusive of McBurney incisions. Even with this reduction in the number of operations, our incidence of eviscerations is only 0.43 per cent, which is about the figure given by von Gusnar and is more than McCauliff's<sup>11</sup> but is less than any of the others.

Of the 32 patients, 10 (31.3 per cent) were men and 22 were women. Our findings in this respect agree with those of Sigalas and are the reverse of those of almost every other investigator. Sigalas and Sokolov definitely listed instances of gynecological conditions among their cases which naturally affected the findings. Unfortunately some of the other authors failed to mention whether they included such cases or not. In our hospital there are approximately twice as many women as men having laparotomies, so this neutralizes the predominance of evisceration in women as compared with men.

The ages of our patients varied from 6 weeks to 65 years, with 70 per cent of them between the ages of 40 and 60.

As to the types of operations after which evisceration occurred, we found in our series that 13 (40.6 per cent) followed hysterectomies, of which 1 was for carcinoma and 1 for sarcoma, 6 cholecystectomies and 4, operations on the stomach, 2 of which were resections for carcinoma and 2 were for the purpose of suturing ruptured peptic ulcers. In our whole series there were 6 cases of malignant disease, 5 of carcinoma and 1 of sarcoma, these constitute less than 19 per cent of our cases. Three eviscerations occurred after cesarean sections. Four occurred in patients operated on for intestinal obstruction.

Just as Sigalas and Stair and Nason noted more instances of incision in the lower part of the abdomen than in the upper part in their group of cases of evisceration, so we noted that 18 (56.3 per cent) of our patients had incisions in the lower part of the abdomen. We found that the median incision is most conducive to evisceration, as 20 of our patients had midline incisions. Of course one wonders what percentage of our total number of operations were made with a midline incision, but, unfortunately, such figures could be obtained only with more labor.

11 McCauliff, G. T. *J. Iowa M. Soc.* 23:347 (July) 1933.

## A REVIEW OF UROLOGIC SURGERY

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*(Continued from page 576)*

### URETHRA

*Valves*—Counseller and Menville<sup>49</sup> stated that congenital valves of the posterior portion of the urethra obstruct the flow of urine and by backward pressure produce renal damage which seriously endangers the life of the patient. Anatomically, the valves may be represented by ridges mucosal folds or fibrous diaphragms covered by mucosa, and the varieties fall into one or more of three types. In type 1, a ridge which divides into two forklike processes is continuous with the verumontanum anteriorly on the floor of the urethra. These processes are thin membranous sheets which extend upward and forward and which may be attached to the urethra through its circumference. In this group is included the nonbifurcated or single type of valve. In type 2 the ridge extends from the verumontanum toward the bladder and divides, similarly to those in type 1, that is, distal to the internal sphincter. Type 3 was first described by Jarjavay, who termed it "iris valve" because of its similarity to the shape of the iris of the eye. The iris valve occurs at various levels and is attached to the circumference of the posterior portion of the urethra. There is usually one opening in the valve, and it varies in size and in position. These three types

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† Deceased

49 Counseller, V S and Menville J G. Congenital Valves of the Posterior Urethra, *J Urol* 34 268 (Sept) 1935

*Essential Details of 32 Cases of Evisceration Following Abdominal Operation—  
Continued*

Patient, Sex, Age	Diagnosis and Operation	Incision	Suture	Postoperative Course	Time of Evisceration (in Days Postop- eratively)	Result Other Condition
21 F M 60	Perforation of cystic duct chole- cystectomy and choledochotomy	Right hypo- chondrium		Normal	9	Good 4+ Wassermann reaction
22 I M 38	Cesarean section	Infra- umbilical				Death
23 M P M 60	Carcinoma of rectum, ileostomy	Infra- umbilical midline	No tension	Wound infection	12	Death hyper- tension arteriosclero- sis, nephritis
24 I R M 60	Gastric carci- noma gastric resection	Midline epigastrie	Tension	Lavage	9	Death broncho- pneumonia
25 D R M 6 weeks	Congenital hyper- trophied colon ceco-tomy	Left rectus		Lavage	6 (2x) 8 (1x)	Death
26 R R F 44	Fibromyoma panhysterectomy	Infra- umbilical midline	Tension	Vomiting	11	Death gallbladder stones, rheumatic heart disease
27 B R I 64	Common duct stone cholecystectomy choledochotomy	Upper right rectus	No tension	Normal	8	Good
28 C S F 43	Fibromyoma panhysterectomy	Infra- umbilical midline	Tension	Lavage	7	Good
29 D S F 37	Chronic cholecystitis cholecystectomy	Upper right rectus		Lavage	7	Death
30 E S F 42	Fibromyoma panhysterectomy	Infra- umbilical midline	Tension	Normal	8	Good
31 A R S M 35	Appendicitis exploratory with appendectomy	Upper right rectus	No tension	Vomiting	4	Death peritonitis cardiac dilatation
32 S W F 63	Distended gallbladder cholecystectomy drain	Supra- umbilical and infra- umbilical midline	No tension	Almost anuric	4	Death

than seems justified by the value of the results. However we feel convinced that the percentage of midline incisions as compared to that of right and left rectus incisions is much smaller than the 62.5 per cent of eviscerations following midline incisions.

We did not feel that the method of wound closure made a great deal of difference, for almost as many types of sutures and methods of closure are used in the Michael Reese Hospital as there are surgeons working. However in all our cases the incision was closed in layers, and in all plain or chromic catgut or both were used for the deeper layers. The skin was closed either with silk or dermal suture or with clips. In only 21 of the cases was there any definite note as to whether tension sutures were used. In 15 of these cases tension sutures were used. We believe that they are of little or no help for in 10 cases

The symptoms of congenital valvular obstruction in the posterior portion of the urethra vary with the degree of obstruction and the presence of infection. In mild cases in which a unilateral valve is present, or when the arrangement of the valves is such as to produce a mild obstruction, there may be no symptoms until infection supervenes. In the majority of cases of urinary difficulty, a small stream, dribbling, frequency and enuresis are common symptoms. Frequency, even in the absence of infection, is common in all but the late stages of the disease because of the reduced elasticity and working capacity of the hypertrophic bladder. When infection is present there are dysuria and urgency. The intensity of the reaction depends on the type of the infecting organism and on the extent of involvement. Bacterial invasion rapidly destroys the renal tissue which has escaped hydronephrotic atrophy, and renal function is proportionately reduced.

The diagnosis frequently can be made from the history. The disease occurs in young male children in whom other types of obstruction below the bladder are uncommon. An intractable puvria in young boys is suggestive of valvular obstruction. In advanced stages the abdomen may be prominent as a result of a dilated bladder, hydro-ureters and hydronephrotic kidneys. There is often residual urine. Cystograms usually demonstrate the presence of a dilated posterior portion of the urethra, and not infrequently remarkable ureterograms and pyelograms are obtained by reflux filling of these dilated structures from the bladder. The differential diagnosis in children includes a consideration of congenital diverticulum of the urethra, congenital stricture of the urethra, congenital hypertrophy of the verumontanum, vesical calculus and contracture of the vesical orifice.

The treatment of congenital valvular obstruction of the posterior portion of the urethra consists of surgical removal of the valves. Trans-urethral removal by means of Young's punch is an effective and simple method. Fulguration through the operating cystoscope and removal by small cystoscopic scissors have been successful in a number of cases. The prognosis depends directly on the amount of permanent renal damage. Renal impairment is the result of increased pressure in the urinary tract, with resulting dilatation of the ureters and renal pelvis and is proportional to the degree and duration of the obstruction in the posterior portion of the urethra.

*Reconstruction*—HARRIS<sup>51</sup> reported 5 cases in which there was complete destruction of the urethra in association with vesicovaginal fistula. Since under the circumstances for which the operation is to be undertaken the sphincter of the bladder and posterior wall of the urethra

<sup>51</sup> Harris, S. H. Reconstruction of the Female Urethra, Surg. Gynec. & Obst. 61: 366 (Sept.) 1935.

postoperative day, 4 were instances of malignant disease. In the other 2 cases of malignant disease evisceration occurred on the eighth and ninth days. As one half of the cases in which evisceration occurred late were instances of malignant disease and as it is the tendency for surgeons to leave skin and tension sutures in longer in such cases than in the average we wonder whether the fact that the wound was closed was not responsible for the apparent lateness of evisceration. Furthermore, it seems to us that this tends to show that the length of time that the skin sutures remain in the wound has actually very little to do with insuring the healing of the wound. This is contrary to Baldwin's belief

	25	26	27	28	29	30	31	32	33	34
J					+			+		+
F	+					+	+	++		
M							+	+		
A						+				
M	++					+				
J					+					+
J						+	++			
A	+					+				
S			+							+
O					+					++
N										
D					+		++			

Chart 2—Incidence of evisceration according to month and year

that the number of his cases of evisceration has decreased owing to the longer period during which he leaves the sutures in situ.

Various authors, notably Meleney and Howes, have expressed the belief that extrinsic factors are important. They stated that cough, wound infection and gastric lavage are of great influence in causing evisceration. We found that in only 4 of the 31 cases on which we have details had wound infections occurred. This incidence is less than 13 per cent. Severe vomiting occurred in 39 per cent of our patients and severe coughing in 16 per cent. Gastric lavage was done in 7 patients, only 22.5 per cent. One patient had a positive Wassermann reaction, 2 had bronchopneumonia, of whom 1 recovered, 1 had diabetes, well controlled, and left the hospital in good condition. Two patients had rheumatic heart disease, 1 of them died suddenly.

of symptoms. The extent of the lesion as compared with the recent development of signs and symptoms is of some diagnostic significance. The symptoms and signs are urinary obstruction, visible tumor and chronic irritation either from infection or from trauma. The majority of the tumors are nonpedunculated, although there is no characteristic appearance in the early stage. Because the symptoms develop late in the disease, microscopic examination should be made of all tumefactions and of all caruncles, ectopions or innocent-looking papillary growths. Late in the disease the outstanding characteristics of carcinoma are induration, ulceration and bleeding and tenderness on palpation. Primary metastasis takes place in the inguinal and pelvic lymph nodes.

The results of treatment by any method are on the whole unsatisfactory. From a review of the reported cases and results in his own, Menville recommended radical extirpation of growths which are not too extensive and complete removal of which is possible. The cases best suited for surgical treatment are those in which the tumor is limited to the anterior portion of the urethra. The inguinal lymph nodes should also be removed surgically. When the growths are extensive and beyond the possibility of complete extirpation, they are probably best treated by small and repeated doses of radium and roentgen rays.

#### GENITAL TUBERCULOSIS

Young<sup>54</sup> presented a series of statistics which are in complete agreement as to the following facts concerning genital tuberculosis. The disease arises more commonly in the prostate gland and vesicles than in the epididymis. Genital tuberculosis is ultimately accompanied by tuberculosis of the lungs or kidneys in a large percentage of cases. If the seminal vesicles are involved, adequate drainage is not furnished by the ejaculatory ducts, and from this region the disease progresses downward to the epididymis or upward to the kidneys or lungs. The presence of renal tuberculosis, which has occurred in about 30 per cent of the cases, is no bar to performing the radical operation in addition to nephrectomy, and curative results may thus be obtained. The presence of old or recent tuberculosis of the lungs is often no contraindication to the radical operation, if possible, arrest of pulmonary tuberculosis should be assisted by removing the external foci of tuberculosis. If the disease is apparently localized within the scrotum, careful examinations should be made to determine that there is no involvement of the vesicles and prostate gland before relying entirely on epididymectomy, which generally will not arrest tuberculosis of the vesicles. Radical removal of the seminal tract, epididymes, vasa deferentia, vesicles and lateral lobes

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<sup>54</sup> Young, H. H. Tuberculosis of the Genital Tract, *J. A. M. A.* 104:722 (March 2) 1935.

when brand B catgut was used it is obviously impossible and unfair to stigmatize this catgut. Both brands incidentally come from firms of the highest reputation. Furthermore it is interesting to note that in both instances the use of brand A was discontinued because the surgeons felt that the incidence of low grade wound infections was increased and that brand B seemed to give less trouble in this respect. In other words, the incidence of eviscerations in our series does not seem to run parallel with that of apparently poorly healing wounds.

#### SUMMARY

Our series of 32 cases represents all the eviscerations occurring in this hospital in the past ten years. During this time 12445 laparotomies have been performed. Subtracting from this number most of the 5262 appendectomies, we find that we have had 32 eviscerations after approximately 7500 laparotomies or an incidence of 0.43 per cent. The mortality rate after evisceration was 37.5 per cent. There were twice as many cases in women as in men but as many more women are operated on than men the sex of the patient apparently plays no role. We found evisceration occurring most frequently after operations on the lower part of the abdomen more often after hysterectomy than after any other type of operation and more often after a midline incision than after other kinds of incision. There were 6 cases of malignant disease in the group. The evisceration occurred most frequently between the sixth and the ninth day postoperatively. We do not feel that the method of wound closure or the length of time that the sutures are in place is of any great significance. Tension sutures apparently play little or no part in preventing evisceration. Complications such as coughing, vomiting, wound infection and frequent gastric lavage, seem to be of relatively little importance. Lastly the sporadic occurrence of our cases of evisceration and their definite grouping at certain irregular intervals are striking.



[COMPILERS' NOTE—Arguments for and against radical operations for tuberculosis of the genital tract have passed back and forth for eighteen years. After following Quinby's results and after performing a number of radical operations for this lesion, O'Connor performs simple epididymectomy, plus hygienic treatment, heliotherapy and tuberculin. At present he employs epididymectomy only in those cases in which continual suppuration causes repeated fistulas or in which heliotherapy and tuberculin do not control the lesions. After having several patients die rapidly of tuberculosis when epididymectomy was done in acutely active cases, O'Connor now insists on several months of administration of old tuberculin plus hygienic treatment before performing epididymectomy.]

Faragó<sup>56</sup> reported a case of primary isolated tuberculosis of the seminal vesicles. The patient complained of bloody semen. On examination the right seminal vesicle was swollen and was sensitive to pressure. Many clumps of tubercle bacilli were found in the seminal fluid. Tuberculosis was not found in the rest of the urogenital system or elsewhere in the bladder. The patient was under observation for three and a quarter years, and the condition remained isolated.

#### HEMATURIA IN PREGNANCY

Morris<sup>57</sup> reported that in a routine study of 154 cases of disturbance of the urinary tract during pregnancy hematuria occurred in 30 cases. Cystitis was present in all of these cases. Pyelitis occurred in 22 cases, in 20 being bilateral and in 2 unilateral. Hydronephrosis occurred in 10 cases, in 2 being bilateral and in 8 unilateral. Pyonephrosis of the right kidney occurred in 2 cases. There was ptosis of the kidney in 9 cases, it was bilateral in 4 cases, on the right side in 4 and on the left in 1. Megalo-ureter was observed in 11 cases, in 4 it was bilateral, in 6 on the right side and in 1 on the left side. There was calculus of the right ureter in 2 cases, and ureteritis was present in 2 cases, in 1 bilaterally and in the other on the right side. Morris concluded that hematuria is a grave complication of pregnancy and that the patient should have a thorough urologic investigation.

#### URINARY INFECTION

Crance and Maloney<sup>58</sup> presented a new treatment for bacilluria of the *Escherichia* variety, in which nitrohydrochloric acid is used. This acid

56 Faragó, Gyorgy. Fall einer primären, isolierten Samenblasentuberkulose. LXI Wissenschaftliche Sitzung der Ungarischen Urologischen Gesellschaft, Ztschr f urol Chir 40 207, 1934.

57 Morris, H. L. Hematuria as a Complication of Pregnancy, J A M A 105.403 (Aug 10) 1935.

58 Crance, A. M., and Maloney, T. W. A New Acid Medication in the Treatment of Bacilluria, J Urol 33 657 (June) 1935.

serve as a general classification but in each there are wide variations. The anomalous valves will become evident at an early age because of their obstructive symptoms. A review of 84 cases in the literature revealed that in 75 per cent symptoms appeared at or before 10 years of age and that in 52 per cent they were evident at or before the age of 5 years.

A valve which obstructs will inevitably produce hypertrophy and dilatation of the vesical wall, dilatation of the ureters and pelvis and atrophy of the renal parenchyma. A funnel-shaped or relaxed vesical outlet and dilatation of the posterior portion of the urethra proximal to the obstruction are other frequent findings. In mature patients and in some young patients valvular obstruction presents a picture on cystoscopic examination which, with the exception of the vesical neck, is similar to that of prostatic obstruction which has been present for some time.

Symptoms may be classed as early and late. The early ones are produced by local obstruction and infection, while the late ones are manifestations of impaired renal function which is secondary to urinary obstruction. In cases in which the condition affects children, fretfulness, loss of weight or failure to gain weight, a protuberant abdomen secondary to a distended bladder and difficulty in starting the urinary stream and in voiding are among the early manifestations, all of which may date back to birth.

Logical interpretation of an accurately taken history and physical examination will lead to proper urologic procedures and usually to a correct diagnosis. In cases of severe urinary obstruction, catheterization of an overdistended bladder is the first procedure, obstruction in the posterior portion of the urethra is the most usual finding.

Treatment is based on the relief of urinary obstruction. If the general condition of the patient is poor, extensive treatment should be postponed and palliative measures should be instituted. In cases in which instruments can be passed into the urethra, the condition should be treated transurethrally in a manner similar to the methods used in resection of the prostate gland.

Landes and Rall<sup>50</sup> stated that the etiology of valvular obstruction of the posterior portion of the urethra is not definitely established. The early anatomists regarded it as being due to dilated lacunae, aberrant folds of mucosa, adherent masses of fibrin which had become organized or inflammatory changes in the mucosa of the canal. The frequent occurrence of such obstruction in infancy and in childhood suggests a congenital origin.

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<sup>50</sup> Landes, H. E., and Rall, Richard. Congenital Valvular Obstruction of the Posterior Urethra, *J. Urol.* **34**: 254 (Sept.) 1935.

to form any definite conclusions, a number of cases have been observed in which there has been marked improvement following its use

#### PYURIA

Briggs<sup>60</sup> presented a review of the literature on so-called aseptic pyuria and reported 3 cases of the condition. Two of the most reasonable views in regard to the etiology are that the infection is caused by a filtrable virus or ultramicroscopic micro-organism and that the gram-positive organisms entrenched in the renal parenchyma cause an inflammatory reaction with an exudation of pus into the renal pelvis. The latter theory is substantiated by the facts that Runeberg found staphylococci in the lesions of kidneys he removed for this condition, that when any organisms were found in the laboratory they were staphylococci and that neoarsphenamine is almost a specific in the treatment of renal infections caused by gram-positive organisms and acted like a specific in these cases. Neoarsphenamine was remarkably effective in the cases of Gross, Neckers, Bumpus and the 3 cases herein reported. Briggs was of the belief that it should be more extensively used in order to prevent nephrectomy in cases of unilateral pyuria and continuous severe suffering in cases of bilateral pyuria. Since neoarsphenamine may cause exfoliative dermatitis, anemia and acute yellow atrophy of the liver, it should not be used until other less dangerous medicines have been tried.

#### URINARY ANTISEPSIS

Heathcote<sup>61</sup> has made a very thorough study of hexamine, from the standpoint, first, of its rate of hydrolysis at different hydrogen ion concentrations and second, of its antiseptic power against various bacteria in urine. In the first part of the study the rate of hydrolysis into formaldehyde was determined with and without standard buffer solutions. All the methods in common use for the estimation of formaldehyde are either rendered invalid by the presence of hexamine or require the use of strong acids or alkalis with or without the use of heat, both of which substances will evidently completely upset the determination of the rate of hydrolysis at a definite  $p_H$ . The method finally adopted was the determination of freed ammonia by indirect titration. Ten series of experiments were performed at different values of  $p_H$ , varying from 0.1 to 7. Each series was carried out at three ranges of temperature: (1) 37°C (7) and 37.5°C (3), (2) 32°C (4) 31.5°C (4) and 30.5°C

60 Briggs, W. T. Neoarsphenamine in So-Called Sterile Pyuria, *J. Urol.* 34:230 (Sept.) 1935.

61 Heathcote, R. St. A. Hexamine as an Urinary Antiseptic. I Its Rate of Hydrolysis at Different Hydrogen Ion Concentrations, II Its Antiseptic Power Against Various Bacteria in Urine, *Brit. J. Urol.* 7:9 (March) 1935.

have been more or less completely destroyed, it is necessary not only to fashion a new urethra but also to provide it with an efficient cut-off muscle. Some tags or bands of tissue are likely to be present in the region of the urethra, especially in postobstetric cases. These should be trimmed off level with the mucosa of the vagina and allowed to heal before the plastic operation is undertaken.

The operation consisted of making a U-shaped incision surrounding the vesicovaginal orifice, the open end of the U terminating at the original site of the external orifice of the urethra. The incision was deepened for about 3 mm, and the wall of the vagina beyond the line of the incision was undermined all around to form lateral flaps. The portion of the vagina embraced by the U-shaped incision was not further disturbed, except by the sutures employed to bring its edges together in the midline to reform the urethral tube. A new sphincter was then fashioned from the muscles of the base of the bladder, and the lateral flaps were sewed together over all, the restoration of the urethra being thus completed. Actually the region of the fistula was covered by three or four superimposed layers, whereas in the lower part of the new urethra only two layers were formed. Suprapubic cystotomy concluded the operation. Urethral drainage was not used. The operation is simple and makes use of principles well known in the plastic surgical operations on the male urethra. The absence of tension leaves little room for failure when reasonable precautions are taken.

*Tumors*—Scheibel<sup>52</sup> reported a case of primary carcinoma of the urethra in a man 71 years old. The growth occurred in the fossa navicularis, and there was metastasis to both inguinal regions. Histologically, the tumor was of squamous cell origin. Its situation was quite unusual, and as Scheibel did not believe that surgical removal would be successful, the growth was treated with roentgen rays. This treatment caused the tumor to disappear and the involved region to heal completely.

Menville<sup>53</sup> reviewed 10 cases of a primary malignant growth in the female urethra, bringing the total reported to 149. The majority of early lesions are located near the meatus, and it is suggested that the para-urethral duct emptying on either side of the external urethral orifice, which is susceptible to infection and trauma, is frequently the point of origin. The average age incidence is 53.4 years.

Carcinoma of the urethra grows slowly, yet the physician usually sees the patient late in the disease because of the relatively late onset

52 Scheibel, Pal. Primärer Harnrohrenkrebs beim Mann! LXII Wissenschaftliche Sitzung der Ungarischen Urologischen Gesellschaft anlässlich der Ungarischen Arztewoche, *Ztschr f urol Chir* 40 209, 1934.

53 Menville, J. G. Primary Neoplasms of the Female Urethra, *Surg, Gynec & Obst* 61 229 (Aug) 1935.

doubtful effect with *B coli-communis* and a considerable effect in the case of *B coli-alcaligenes*, six hours' exposure produced a doubtful effect in the case of *Staph aureus*, but a well marked action on the other organisms, (3) at  $p_H$  5 the growth of *Staph aureus* was definitely reduced by six, but only doubtfully by three, hours' exposure, in the case of the other organisms the acidity of the medium itself was sufficient to obscure the effect of hexamine, (4) similar experiments with borax, in a dilution of 1 500 and at  $p_H$  8.5, showed no effect to be produced on *Staph aureus* but a considerable reduction in growth in the case of the other organisms

Two factors are of the greatest importance in the question as to whether an antiseptic strength of formaldehyde will be reached in the urine of a patient taking hexamine time and the reaction of the urine. In cases of infection of the upper part of the urinary tract there will not be sufficient time for such a strength to be developed. In cases of acute cystitis, urine sufficiently acid to produce such a strength of formaldehyde will cause such pain and frequency of micturition as to prevent any effective action. In cases of chronic cystitis there may be hope of reaching an antiseptic strength of formaldehyde over a period long enough to be effective. Hexamine might be a valuable prophylactic in cases in which repeated catheterization is needed. Borax might be of value in the treatment of acute or chronic cystitis, especially if due to a coliform organism.

#### UROGRAPHY

Cahill<sup>62</sup> stated that tumors and enlargements of the adrenal glands have been diagnosed by roentgen examination, either through the density of the shadow made by the tumor itself or through displacement by the tumor of some shadow-forming organ, such as the kidney.

Langeron in 1929 showed that intraperitoneal injection of air would permit visualization of an adrenal tumor. Since 1930 Cahill has used injections of gas after the manner of Carelli for the determination of pathologic conditions in the renal region. This has been of value in cases of tumor adjacent to the kidney, particularly for tumors of adrenal origin. At first the method used was that described by Carelli, with the introduction of a measured amount of gas by transferring fluid from one cylinder to another, driving the measured amount into the perirenal space under a definite known pressure of gravity. This was modified by using air instead of carbon dioxide, and the procedure was simplified by using a manometer in the manner of introducing air into the pleural cavity. The method was further simplified by straight

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<sup>62</sup> Cahill, G. F. Air Injections to Demonstrate the Adrenals, *J Urol* 34: 238 (Sept) 1935.

of the prostate gland is the operation of choice in the treatment of genital tuberculosis

Braasch,<sup>55</sup> in discussing genital tuberculosis, stated that the operation for this lesion which is described by Young, and when performed by him, is a procedure that is worthy of serious consideration. Whether the average urologic or general surgeon can do as well is open to question. This is evidenced by the fact that although not many such operations have been performed, Braasch has observed 3 patients operated on elsewhere who came because of a permanent urethrorectal fistula. Care must be taken also in advising an operation that even in the most skilful hands has an immediate and late mortality as high as is shown by Young's figures. In the first place it must be decided whether so radical an operation for pangenital tuberculosis is necessary. It is well known that evidence of some form of genital tuberculosis is present in the majority of cases of renal tuberculosis. Among 1,200 patients operated on for renal tuberculosis at the Mayo Clinic, evidence of involvement of the genitalia was discovered on clinical examination in approximately 80 per cent of the cases. Surgical treatment has usually been found advisable only in the epididymis or in the testis. The tuberculous epididymis or testis should be operated on mainly because of the common tendency to suppuration and the formation of abscess. In contrast suppuration of the prostate gland or seminal vesicles is rarely observed. The late mortality following nephrectomy for renal tuberculosis in cases of evident involvement of the prostate gland and seminal vesicles is no higher than in those without such involvement. Tuberculosis of the epididymis is arrested by heliotherapy in many cases, as has been shown by a number of observers. The difficulty in advising patients to use heliotherapy is that of securing adequate irradiation. Furthermore, extension of the disease in the epididymis with involvement of the testis is sometimes observed in spite of ideal irradiation. Braasch has observed that the tuberculous epididymis is best removed surgically before suppuration takes place and that heliotherapy should be employed as an adjunct. In this way suppuration and involvement of the testis can be obviated. Reexamination in cases in which tuberculosis of the prostate gland and seminal vesicles was found five or ten years later shows that nature has taken care of these tissues. Rectal examination usually reveals small evidence of previous infection. In some instances cicatricial areas may be felt, in others, the prostate gland and vesicles seem to have atrophied. In only an occasional case is there any evidence of an active tuberculous process. The burden of proof still rests with Young in showing that the late mortality following complete removal of the genitalia is any better than when they are left alone.

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55 Braasch, W. F., in discussion on Young.<sup>54</sup>

be recognized, however, that it is only another diagnostic procedure, and its findings should be checked as far as possible by retrograde cystoscopy. Intravenous injections of urographic mediums are found valueless in severe cases of pyelitis of infancy, as there is no excretion of the medium owing to the pyelonephritis. This test will supplement and make valuable the routine health examinations. At present the general practitioner only examines the urine chemically and occasionally palpates the kidney. In the future he will make intravenous urograms and find lesions which necessitate surgical intervention in their early stages.

Dos Santos<sup>64</sup> described his method of arteriography for the diagnosis of renal and adrenal tumors. Arteriography is an aid and may be the deciding factor in making a differential diagnosis, especially in obscure cases. The aortographic diagnosis is based on the course, extension and number of the renal arteries. Accurate knowledge of the normal anatomic situation is essential for the successful judging of the picture obtained. Impressive examples are offered of the differential diagnosis of hypernephroma, cancer and angioma. In hypernephroma the affected parenchyma does not contain vessels, in carcinomatous kidneys the vessel channels and the width of the arteries are irregular, partly formed new blood vessels are seen, and in some areas the eroded vessels form small lakes of blood. In 1 case, because of unusually numerous and ramifying vessels, a diagnosis of bilateral renal angioma was made, which was verified at operation. In another case, in which a clinical diagnosis of new growth had been made, arteriography showed that only an arteriosclerotic nephritis was present. The picture of the vessels in this condition is very characteristic. In cases of suprarenal tumor it is possible for a skilful technician to note the typical displacements and determine between retroperitoneal growths and hepatic or splenic enlargements. Cases of echinococcus cyst of the liver, sarcoma of the spleen and splenic cyst are discussed.

#### STATISTICS ON UROLOGIC SURGERY

Counseller<sup>65</sup> reported that at the Mayo Clinic in 1934, 1,636 operations were performed on the genito-urinary tract, consisting of 2,343 surgical procedures on 1,403 patients. There were 23 deaths, a mortality of 1.6 per cent. These figures represent an increase of 16.6 per cent in the number of patients and 34.5 per cent in the number of surgical procedures over that of the preceding year. This is accounted for

<sup>64</sup> Dos Santos, Reynaldo. L'aortographie dans les tumeurs renales et para-renales, *Arch d mal d reins* 8 313, 1934.

<sup>65</sup> Counseller, V. S. A Survey of Surgical Urology for 1934, *Proc Staff Meet, Mayo Clin* 10 515 (Aug 14) 1935.

reduces the  $p_H$  to 5 or below in apparently less time than the ketogenic diet and can be administered to the patient without the need of hospitalization and without change in the ordinary diet. So far, urinalysis, regularly done in all cases, has failed to show any renal damage by consistent absence of albumin and casts. In 1 of the cases reported in which the ketogenic diet failed utterly, the patient recovered completely under treatment with nitrohydrochloric acid. Crance and Maloney stated that it has been their custom to continue this treatment for approximately one week after culture of the urine has become sterile.

Braasch<sup>59</sup> stated that the usual methods employed in combating persistent urinary infections, including medication with so-called urinary antiseptics, the administration of vaccines and serums and the use of bacteriophage, are in most cases unsatisfactory. The discovery by Helmholtz and Clark of a method of inhibiting bacterial growth in the urine by means of ketosis and acidification has given an accurate and scientific method of treatment. The therapeutic value of ketosis in the treatment of bacillary infections of the urinary tract has been established by experience with several hundred patients in the past three years at the Mayo Clinic. Although the establishment of ketosis is the major portion of the treatment in many cases of infection of the urinary tract, it is often inefficient unless aided by other therapeutic measures. In the majority of cases the critics of the ketogenic diet, who have failed to obtain satisfactory results, have overlooked the following factors: meticulous administration of the diet, complete elimination of persistent foci of infection and attention to the presence of a mixed infection, which requires methods of treatment other than the ketogenic diet. Even in its present simplified form it is questionable whether treatment with the ketogenic diet should be attempted unless the diet is controlled by some one familiar with dietary regimens and the patient is kept under daily observation. One of the most significant obstacles to successful treatment of bacilluria is caused by reinfection from a persistent prostatitis. Frequently usual methods of treatment, consisting of prostatic massage, dilation of the urethra and deep instillations, are unsatisfactory in eliminating this focus of reinfection. In accordance with the suggestions of Grant, attempts have recently been made at the Mayo Clinic to control prostatic infection by intraprostatic injections of mercurochrome. In one case, on two occasions 10 cc of a solution of mercurochrome was injected into the prostate gland, and apparently this was a definite factor in diminishing the degree of prostatic infection. Although experience with this type of injection has not been sufficient

<sup>59</sup> Braasch, W. F., in discussion on Control of a Severe Form of Chronic Pyelonephritis and Prostatic Infection by the Ketogenic Diet, Proc. Staff Meet., Mayo Clin. 10:596 (Sept. 18) 1935.



incontinence because of anomalous ureter. Transplantation of the ureter was performed in 8 cases: in 4 of exstrophy, in 2 of interstitial cystitis, in 1 of cystitis and contracted vesical neck, and in 1 of epispadias. This operation is of value when more conservative methods are not practicable for the treatment of severe vesicovaginal fistulas, particularly those produced by application of radium to carcinoma of the cervix, and in an occasional case in which the floor of the pelvis and neck of the bladder have been damaged beyond repair by parturition. The mortality is about 5 per cent, so that the operation should not be denied any patient for whom it is definitely indicated.

Among 356 patients with conditions of the kidney treated surgically there were only 7 deaths. Frequently complicating conditions modified the standard treatment. The cases were divided into groups: nephrolithiasis with or without hydronephrosis, pyelonephritis or pyonephrosis, hydronephrosis without stones, malignant lesions of the kidney, and miscellaneous renal conditions. In the first group there were 122 cases. In 26 of these one kidney was functionless or so damaged that nephrectomy was performed. Stones, single or multiple, were removed from the renal pelvises of 78 patients without fatality. Forty patients who had hydronephrosis without stones were subjected to 67 surgical procedures. In such cases conservative or restorative operations are indicated because not infrequently the lesion is bilateral and often one kidney has been removed for a similar condition. In 21 cases, approximately 50 per cent, the involved kidney had been partially obstructed so long that it was functionless and nephrectomy was carried out. If the condition involved the other kidney, either a plastic operation on the renal pelvis or permanent nephrostomy was done. Nineteen patients underwent single or multiple conservative operations for various degrees of hydronephrosis.

Twenty-eight patients with malignant lesions of the kidney underwent nephrectomy; of the lesions, 15 were hypernephromas. There were 5 children with Wilms' tumors. The other lesions were hemangio-endothelioma, epithelioma and sarcoma. In 1 case there was an extensive primary carcinoma of the adrenal gland, the kidney was adherent to it, and since the lesion was of grade 4, the kidney was removed together with the tumor. In this case clinical symptoms characteristic of adrenal tumor were absent.

On the external genitalia 799 surgical procedures were performed for cryptorchidism, hypospadias, epididymitis, tumor of the testis, varicocele, hydrocele and phimosis or redundant prepuce. Fifty-nine of these procedures were done on 35 patients with cryptorchidism. The Torek and Cabot operations continue to be the procedures of choice and were performed on 27 patients. The Cabot operation is indicated

(2), and (3) at room temperature, varying from 29.5 to 23 C. In the first three series, at  $p_H$  0.1, 0.4 and 0.8, respectively, no buffering substances were employed. In the remainder, standard buffer solutions were used.

Heathcote concluded that (1) In solutions of  $p_H$  from 0.1 to 1.1, the hydrogen ion concentration is the determining factor in the rate of the hydrolysis, the velocity constant for the reaction varying directly with it, (2) in solutions not more acid than about hundredth-normal, the velocity constant is not solely dependent on the hydrogen ion concentration, being far greater than would be expected if the relation mentioned in the previous paragraph held good, and (3) this may probably be accounted for by (a) the presence of neutral salts in the buffered solutions, and by (b) hydrolysis being partially brought about by the undissociated fraction of acid salts there present.

The second part of the study dealt with the antiseptic power of hexamine against various bacteria in the urine. This depends largely on the ultimate strength of formaldehyde in the urine at any definite point. It will be determined by the percentage of hexamine present, which in turn depends on the dose administered, the proportion of that dose which is destroyed elsewhere in the body and the volume of urine secreted. With a known amount of hexamine present in the urine the amount of formaldehyde will depend on (1) the hydrogen ion concentration of, and the amount of neutral and acid salts present in, the urine, and (2) the time factor, in that during the continuous process of the secretion of urine each molecule of hexamine is exposed to the hydrolytic process in acid urine from the moment of its excretion by the kidney until it is finally voided. A further important point is the time required by a definite concentration of formaldehyde to kill any given organism or the strength required to prevent the growth of that organism. Three strains of bacteria, *Staphylococcus aureus*, *Bacillus coli-communis* and *Bacillus coli-alcaligenes*, each recently isolated in a case of infection of the urinary tract, were used. Three sets of experiments with hexamine were performed, at  $p_H$  5, 6 and 7, respectively, while a fourth was carried out at  $p_H$  8.5, borax being used in place of hexamine. Each of these sets was duplicated by using as a medium in the one case an aqueous buffered solution and in the other urine, both brought to the desired  $p_H$ , which was checked by the use of indicators.

Heathcote found that the effect of exposure at 37 C. for periods of three and of six hours of *Staph. aureus*, *B. coli-communis* and *B. coli-alcaligenes* to a 1:500 solution of hexamine at  $p_H$  5, 6 and 7 was as follows: (1) at  $p_H$  7, no definite effect on the growth of any of these organisms could be observed even after six hours, (2) at  $p_H$  6, three hours' exposure produced no effect in the case of *Staph. aureus*, a

Cabot<sup>67</sup> noted the different development of operations for transplantation of the ureters to the intestine in this country as compared with those in Europe. In the latter a number of the best known experts have largely abandoned the operation because of the high mortality, which is from 25 to 35 per cent. In contrast to this, there are cases such as those reported from the Mayo Clinic by Walters in which in a series of approximately 100 cases there has been a mortality of less than 5 per cent and excellent results have been obtained. It is Cabot's opinion that this difference is due to the selection of cases. Many of the European operators have used uretero-enterostomy for patients with badly damaged ureters and commonly for patients with cancer of the bladder, who are obviously unsatisfactory risks. The most favorable results from this operation can be expected only when performed on substantially normal ureters and on patients in relatively normal general condition. The transplantation of the abnormal ureter or the transplantation of the practically normal ureter of an extremely debilitated patient will not give satisfactory results. If these limitations are taken into consideration, the evidence warrants the assertion that uretero-enterostomy has achieved a permanent position, although it need not be assumed that it will generally leave the patient with entirely normal kidneys for the rest of his life.

#### UROLITHIASIS

Reaser<sup>68</sup> studied a series of approximately 5,900 reports of necropsies to ascertain the incidence of urolithiasis and to compare the prevalence of stones in the white and Negro races. Seventy-nine cases of urinary calculi were recorded, in 14 of which the patients were Negroes. Data were not available to determine the ratio of Negroes to white persons in the complete necropsy series. No stone was found in a Negro less than 50 years of age, and the majority were 60 years or older. In practically all cases in which stones were found a disease process in the kidneys either preceded or accompanied lithiasis. The conclusion is that urolithiasis is uncommon in Negroes and that when it occurs the patient is at an advanced age.

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<sup>67</sup> Cabot, Hugh, in discussion on Walters<sup>66</sup>

<sup>68</sup> Reaser, E. F. Racial Incidence of Urolithiasis, *J. Urol.* **34** 148 (Aug) 1935

injection of the measured amount of air directly into the perirenal space by hand pressure, with no attempts to measure the amount of pressure. It was then ascertained that the injected air could be displaced in the desired direction by manual pressure and that the air would more or less slowly infiltrate through the fascial planes, so that roentgenograms taken twelve, eighteen, twenty-four or thirty-six hours later would show the organs and fascial planes clearly, especially around the adrenal gland. This method has been found to be of value in demonstrating both pathologic and normal adrenal glands. Tumors of the adrenal gland, such as adenoma and carcinoma, as well as hypertrophied bilateral adrenal glands, have been shown. Of special value is the determination of a normal adrenal shadow on the opposite side when an adrenal tumor is present.

No ill effects have resulted from the procedure. There are no particularly large vessels in the area of injection. Whether the trochar is in a blood vessel may be easily determined by aspiration. The introduction of air produces a slightly uncomfortable feeling of pressure, which rapidly disappears. The air at times works down into the psoas fascia and has produced some crepitation in the thigh over Scarpa's triangle, but this usually disappears in a few days.

With the patient on his side, the area of the flank is sterilized. Procaine hydrochloride is injected into the site of the injection as well as into the tract. The trochar is then introduced, usually below the twelfth rib, in an area between the outer border of the erector spinae muscle and the reflection of the peritoneum. As the trochar passes through the transversalis fascia the change in resistance is noted, it is then passed a short distance upward and inward. At this point changes in manometer readings on inspiration and expiration show whether the open end of the trochar is in the renal fascia. Attached to the trochar is a sterile glass tube filled with sterile cotton which acts as an air filter. This is further connected to a rubber bag and then to a measure pump. Between 200 and 250 cc of air, depending on the size of the patient, is introduced into the bag and is then slowly forced by hand from the bag through the cotton and trochar into the perirenal fascia. A film is then taken and developed. This shows where the air is located. It then may be displaced upward or downward in the fascial planes by manual pressure. The films that have most satisfactorily shown the fascial planes have been those taken eighteen or twenty-four hours later. In these the air has been well diffused.

Wesson<sup>63</sup> stated that intravenous urography has restored a large portion of the field of medicine to the general practitioner. It should

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63 Wesson, M. B. Intravenous Urography for the General Practitioner, South M. J. 28:16 (Jan) 1935.

Subjects were lightly clothed and were always in the room for thirty minutes before the measurements were started in order to adjust themselves to the environmental temperature and humidity. To remove any moisture already on the skin or in the tubing, the dry air was passed for twenty minutes before collections were made. Several successive collections were made from each area studied, and whenever possible determinations were made not only from the burned area but also from a corresponding normal area. The determinations were repeated daily at the same hour until the burned area seemed to be normal again.

The rates of evaporation from the burned and normal areas must be considered relative rather than representative of the actual rates that would prevail outside the laboratory, since the air used in the experiment was dry and moving. Vasti<sup>1</sup> found that both humidity and cutaneous temperature within certain limits affect the local evaporation from the skin. Similarly, the temperatures of the skin measured inside the capsule are not accurately characteristic of the normal surface, but with uniform rates of air flow the values have relative significance.

*Control Procedures*—Control measurements made on normal persons during the present study showed a maximum difference of 20.8 per cent and an average difference of 8.4 per cent in 100 pairs of successive determinations on many different subjects. Variations in different parts of the body of the same person were considerable, the forehead having the greatest rate of evaporation, 0.0686 mg per square centimeter per minute, and the extensor surface of the forearm having the least, 0.0343 mg per square centimeter per minute. The mean for the entire body was 0.0454 mg per square centimeter per minute, or 27 Gm per square meter per hour. The evaporation was greater from flexor surfaces, owing possibly to the fact that more sweat glands are present per unit of area on flexor surfaces and that the texture of the skin is finer. The greatest variation on different days in the rate of evaporation from corresponding areas was 43 per cent, and the mean difference was 11.8 per cent.

In some cases the presence or absence of activity of the sweat glands was determined microscopically in the manner suggested by Jurgensen.<sup>2</sup> A drop of liquid petrolatum containing 2 per cent methyl red was placed on the skin and observed under a microscope. If the sweat glands were active, the brighter droplets of sweat as they formed could be observed against the darker background of the red oil.

Mild first degree burns were produced on normal volunteers by exposure to ultraviolet radiation from a quartz mercury vapor arc lamp. The rates of evaporation and the cutaneous temperatures were followed just as in the clinical cases. Like determinations were made following the application of tannic acid to normal skin.

## RESULTS

*Rates of Evaporation*—These were measured at the same time of day for many successive days. That the differences from normal were consistent is shown by chart 1, which represents data on one of six subjects in whom first and second degree burns were studied simultaneously. Chart 2 shows a composite graph of the rates of evaporation in eight cases of second degree burn, before and after the application of tannic acid.

In the majority of cases, before the application of tannic acid the rates of evaporation were found to be high, sometimes as much as 400 to 500 per cent as

1 Vasti, A. The Insensible Water Loss Through the Skin, *Am J Physiol* **102** 60, 1933.

2 Jurgensen, E. Mikrobeobachtungen der Schweissekretion der Haut des Menschen unter Kontrast-Färbung, *Deutsches Arch f klin Med* **144** 193, 1924.

by the increase in the number of patients presenting themselves for transurethral resection of the prostate gland

In cases of carcinoma of the bladder the most effective operation is total removal of that organ, provided the carcinoma is confined within its walls, with transplantation of the ureters either to the sigmoid colon or to the skin. The latter procedure is safer than the former, but the patient is disturbed considerably by the constant presence of urinals on the thighs. Grading of tumors of the bladder is sound fundamentally, and, as Keyes has stated, all epithelial tumors of the bladder graded 1 or 2 should be regarded as curable and should be treated by fulguration or implantation of radon, or by cystectomy or other operative procedures. The prognosis for lesions of grade 3 and 4 is poor after any surgical method. Highly malignant lesions, with a base measuring more than 2 cm in diameter, are practically hopeless no matter what surgical attack is used. During 1934, 61 patients with carcinoma of the bladder were treated by 71 major surgical procedures, consisting of segmental resection, fulguration, cautery, application of radium, excision, ureterosigmoidal anastomosis, total cystectomy and ureterostomy. Every available method was utilized, and in each instance the method of attack was governed largely by the size, situation and grade of malignancy of the tumor. The most satisfactory results were obtained in cases of small lesions of a low grade of malignancy. Twenty-three patients were treated by combined excision, electrocoagulation, cautery and the application of radium, 14, by segmental resection, and 6, by segmental resection and reimplantation of the involved ureter. There were 4 deaths in the entire group. The lesions in these cases were graded 4 in 3 cases and 3 in 1 case. All of the lesions were extensive and confined to the region of the trigon and vesical neck. It is generally agreed that for small lesions of a low grade of malignancy the transurethral approach is satisfactory, but for more extensive lesions of a low grade and for all lesions of higher grades of malignancy the suprapubic approach should be used. If such lesions are confined to the mucosa or portions of the wall, the possibility of cure is good. If a case is suitable for bilateral ureterosigmoidal anastomosis and total cystectomy, complete removal of the bladder seems necessary. However, if a ureter has been damaged by obstruction and infection, the risk is too great to justify the procedure. It is safer to perform bilateral cutaneous ureterostomy and cystectomy.

In 1934 it was necessary to remove stones from the ureters by ureterolithotomy in 40 cases. Other surgical procedures on the ureter consisted of ureterotomy and ureterostomy for tuberculosis, either of the ureter or of the bladder, plastic operations on the ureter for obstruction and transplantation of the ureter into the bladder for urinary

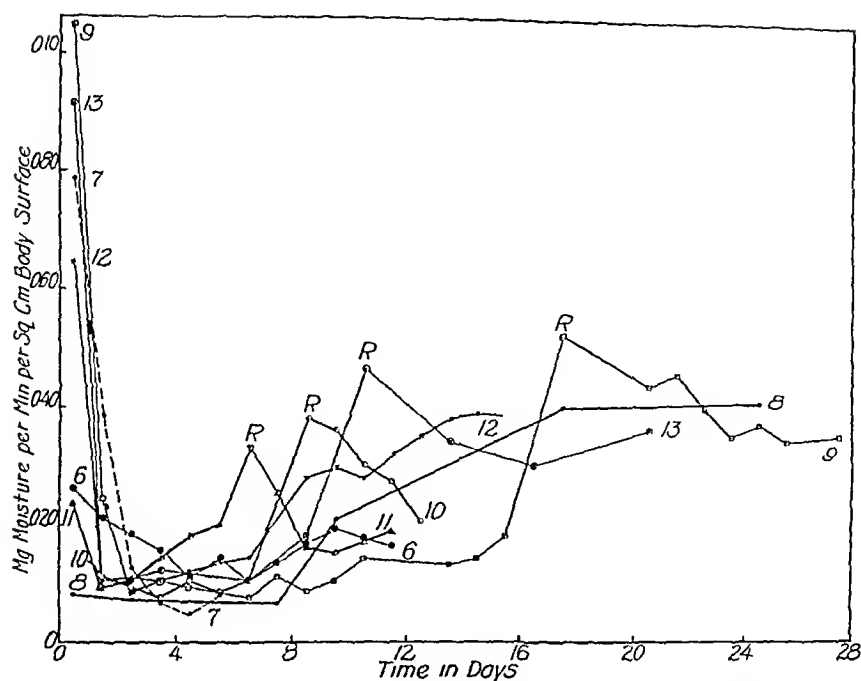


Fig 2—Rates of evaporation of water from areas of second degree burns. In each case the burn occurred on the first day of the experiment, and the measurements recorded on that day were obtained before treatment with tannic acid was begun. Tanning was usually completed before the second day's measurement. At *R* the eschars were removed.

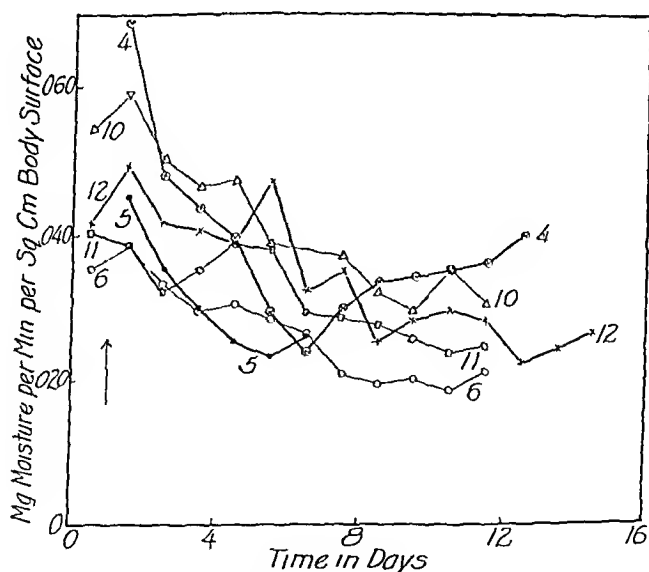


Fig 3—Rates of evaporation from areas of first degree burns. In each case the burn occurred on the first day of the experiment.

if the spermatic cord is of adequate length, if the scrotum is fairly well developed and if it is desired to maintain temporary traction while the patient is in the hospital. Good results from the Torek operation were obtained in approximately 95 per cent of cases. Orchidectomy was performed on 10 patients with malignant lesions of the testis. Some others were treated only with roentgen rays. Some received roentgen treatment prior to operation, and all received it after operation. At present quantitative estimation of excretion of a follicle-stimulating hormone in the urine is not a sufficiently accurate index of the histopathologic characteristics of a tumor. The technic of orchidectomy is such that the operation can hardly be contraindicated in any case, the primary tumor is not only removed, but the type of tumor cell present can be determined. The discovery that this hormone is excreted in the urine of men who have malignant lesions of the testes and not in that of other men has added much to the knowledge of this disease. The greater the amount of hormone excreted the higher the grade of malignancy. Furthermore, if the rate of excretion is affected little by roentgen therapy and if the rate of appearance in the urine is persistently high, the prognosis is poor.

Walters<sup>66</sup> stated that the early plastic operations for hydronephrosis were developed by Kuster, Trendelenburg, Bazy and Christian Fenger. Several successful operations of the Fenger type were performed at the Mayo Clinic for hydronephrosis prior to 1920. Approximately 75 plastic operations for hydronephrosis have been performed at that institution since 1927. Some of the procedures used in these cases have been resection of the hydronephrotic renal pelvis, reimplantation of an abnormally placed ureter into a hydronephrotic renal pelvis and, in 1 case, ureteropyeloneostomy. Removal of infected portions of duplicated kidneys affords a suitable field for conservative renal surgical treatment.

Another field for transplantation of the ureters to the sigmoid is in cases of contracted bladder following removal of a tuberculous kidney. Submucosal transplantation of the ureter into the sigmoid was performed in 2 such cases, in 1 for a contracted bladder caused by tuberculosis and in the other for diffuse submucosal inflammation of the bladder. Uretersigmoidal transplantation may be used in selected cases of inoperable carcinoma of the bladder in which total cystectomy is to be performed. Its main application is in cases of exstrophy of the bladder, more than 100 patients with this type of lesion have been operated on at the Mayo Clinic.

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66 Walters, Waltman. Plastic Operations on the Genito-Urinary Tract. I. Operation on the Ureters and Kidneys, Proc. Staff Meet., Mayo Clin. **10** 529 (Aug. 21) 1935.



found that in a person with congenital absence of sweat glands the insensible loss of moisture at rest was as great as that of a normal person

*Frost-Bite*—This was studied in the same manner in two cases in which tannic acid therapy was applied. In one case both feet were affected, in the other one foot served as a normal control. The rates of evaporation and the cutaneous temperatures were very high at first, fell markedly after the application of tannic acid and then rose gradually to normal. The results were precisely similar to those in cases of second degree burns

*Burns Caused by Ultraviolet Radiation*—Burns caused by ultraviolet radiation of the skin were studied in two normal persons on four occasions. The rates of evaporation were always abnormally low immediately after the exposure, but a few hours later they began to rise (chart 4), and by the following day they were (in experiment 4) as much as 200 to 300 per cent above the values for the corresponding normal areas. As the area healed, there was a gradual return to the normal level that had been observed before the treatment. When the dead skin peeled off,

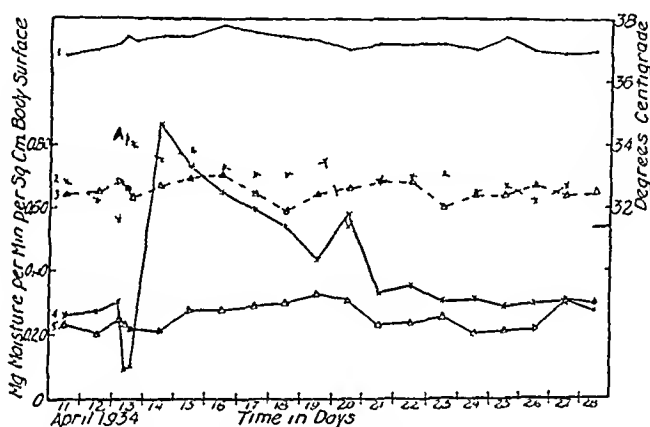


Fig 4 (experiment 4, subject G S M) —Temperatures and rates of evaporation of water from the flexor surfaces of both forearms, the left being burned once with ultraviolet radiation. Line 1 indicates the rectal temperature of the subject, line 2 indicates the temperatures of the irradiated area, and line 3 indicates those of the corresponding normal area. Line 4 indicates the rate of evaporation from the irradiated area, and line 5 indicates that from the corresponding normal area. Irradiation occurred at A.

the rate of evaporation rose markedly for a day or two and then fell again. The cutaneous temperature in general rose and fell with the rate of evaporation. Tannic acid did not form a coagulum over these areas and seemed to have no effect on the rate of evaporation, such areas resembling, therefore, first degree accidental burns.

The temporary inhibition of evaporation immediately following exposure, which was found in all four experiments, might have been due to some direct effect of the radiation on cellular activities or on the superficial blood vessels. This decrease in the rate of evaporation may be a contributing cause of the fever associated with sunstroke, since it indicates that loss of heat is retarded, at least in part.

## EVAPORATION OF WATER FROM SUPERFICIAL BURNS

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The object of the experiments was to answer the questions: Does evaporation from burned surfaces account for a significant portion of the dehydration of the body that is believed to be present after accidental burns? Does the treatment of these surfaces with tannic acid materially modify this evaporation?

### METHOD

*Apparatus*—A glass capsule was fitted with inlet and outlet tubes opposite one another. It enclosed an area of skin of 22 sq. cm. A thermocouple on the end of a piece of bakelite tubing was held inside the capsule, so that it was pressed lightly against the surface of the skin at all times. Wires to a cold junction and to a galvanometer passed through the tubing and the sealed top of the capsule. The capsule was sealed air-tight to the cutaneous surface with petrolatum. A stream of air was measured by passage through a dry meter, was dried by passage through a spiral washing-bottle containing concentrated sulfuric acid and was drawn through the capsule by suction. Tests were made for leaks around the capsule by pinching momentarily the tubing that led the air into the capsule.

The moisture acquired by the air while in the capsule was collected in weighed flasks of concentrated sulfuric acid during ten minute periods. The flow of air was approximately constant at 0.5 liter per minute, but variations in the flow from 0.2 to 3 liters per minute produced no significant changes in the rate of evaporation. Rates of evaporation were calculated as milligrams of water per minute per square centimeter of surface.

Blank measurements with a dry glass plate in place of the cutaneous surface showed an average gain by the collecting flasks of 0.5 mg. in ten minutes. Since the average amount of moisture picked up from the skin in any one determination was 10 mg., the error was 5 per cent.

Cutaneous temperatures were determined with the thermocouple from the readings of a galvanometer and of a mercury thermometer at the cold junction, which was immersed in a thermos bottle of water at approximately 26 C.

*Conditions*—The measurements were carried out in a room in which the temperature was controlled within  $\pm 1$  C. and the humidity within  $\pm 8$  per cent, with a mean temperature of 26 C. and a mean relative humidity of 50 per cent.

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This investigation was supported in part by the Fluid Research Fund of the Rockefeller Foundation. The patients studied were in the Strong Memorial Hospital and the Rochester Municipal Hospital.

the spaces in various tissues<sup>8</sup> Restoration of the normal distribution of fluid, then, depends on vascular and other readjustments within the body

It has been shown by Landis<sup>9</sup> that several types of hyperemia, such as those produced by heating the skin, increased the pressure within the capillaries of the skin It is likely that the tendency of fluid to leave the blood stream that results from this increase of pressure has something to do with hastening evaporation from the surface

When tannic acid was first introduced into the therapy of burns,<sup>10</sup> the belief was widely held that by coagulating the burned tissue it prevented the absorption of poisonous products and thus lessened the toxemia<sup>11</sup> Underhill,<sup>12</sup> working with rabbits, offered evidence to contradict this hypothesis He found that the absorption of certain dyes from the untreated burned surface was markedly retarded as compared to that from normal skin and that the extracts of burned skin and normal skin when injected into test animals produced like reactions He explained the apparent toxemia on the grounds of altered circulatory relationships produced by concentration of the blood<sup>6</sup>

Underhill and his associates<sup>8b</sup> and Blalock<sup>8a</sup> showed that after experimental burns in anesthetized animals edema fluid rapidly accumulates in adjacent tissues and that this fluid has essentially the same composition as blood plasma In human beings this fluid forms large blebs, and some escapes, but in dogs, owing to the peculiar anatomy of the skin, it does not escape but is reabsorbed Blalock found that the average total amount of fluid lost into inflamed tissues in eighteen dogs which had been burned over one-half the surface of the body was 57 per cent of the volume of the blood

Treatment of burns with tannic acid reduces evaporation enormously, but the belief that the beneficial effects of tannic acid are due to the prevention of loss of water from the body is not supported by the data now available Whatever water and protein are lost from circulation appear to remain largely within the body

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8 (a) Blalock, A Experimental Shock The Importance of the Local Loss of Fluid in the Production of the Low Blood Pressure After Burns, *Arch Surg* **22** 610 (April) 1931 (b) Underhill, F P, Fisk, M E, and Kapsinow, R The Extent of Edema Fluid Formation Induced by a Superficial Burn, *Am J Physiol* **95** 325, 1930

9 Landis, E M Micro-Injection Studies of Capillary Blood Pressure in Human Skin, *Heart* **15** 209, 1930

10 Davidson, E C Tannic Acid in the Treatment of Burns, *Surg, Gynec. & Obst* **41** 202, 1925

11 Martin, J D, Jr Tannic Acid Treatment of Burns, *South M J* **26** 321, 1930

12 Underhill, F P, and Kapsinow, R The Alleged Toxin of Burned Skin, *J Lab & Clin Med* **16** 823, 1931, footnote<sup>6</sup>

compared with those from a corresponding normal area. Following the application of tannic acid the rates of evaporation fell rapidly, reaching a subnormally low level when the area was fully tanned. In case 8, the burn had been caused by boiling paraffin, while in cases 6 and 11 petrolatum and ointment had been applied prior to the patient's admission to the hospital. Traces of these substances remaining on the skin probably inhibited the evaporation and caused the comparatively low initial rates observed in these particular cases.

The rates of evaporation remained at the subnormal levels for five or six days and then began to rise gradually. In most cases after the removal of the eschars the rates rose markedly to high levels and then dropped gradually to constant rates.

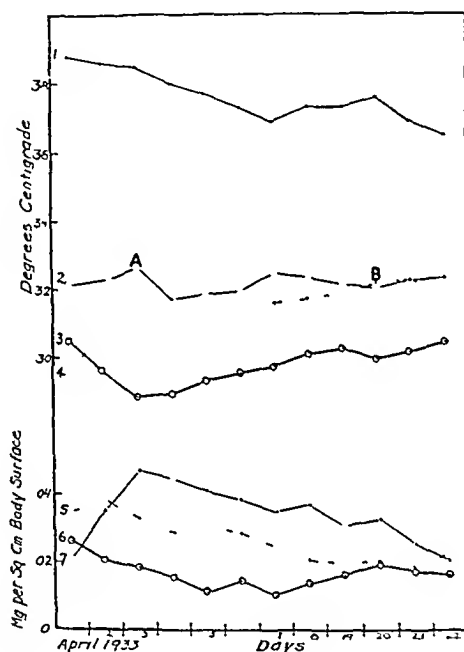


Fig 1—Temperatures and rates of evaporation in a patient burned on the back on April 11. Rates of evaporation are expressed in milligrams of moisture per minute per square centimeter of body surface. Line 1 indicates the rectal temperatures, line 2 indicates the temperatures in a corresponding normal area, line 3 indicates the temperatures in an area of second degree burn, and line 4 indicates those in an area of first degree burn. Line 5 indicates the rates of evaporation from an area of first degree burn, line 6 indicates the rates of evaporation from an area of second degree burn, and line 7 indicates those from a corresponding normal area. Treatment with tannic acid was stopped at A, and the eschars were removed at B.

slightly below normal. In all cases the evaporation from an area completely regenerated after a second degree burn was less than that from the corresponding normal area.

Chart 3 is a composite graph of the rates of evaporation in six cases of first degree burn. In all, the initial rates were abnormally high and gradually decreased

# CONSERVATIVE AND RADICAL MEASURES FOR TREATMENT OF ULCER OF THE LEG

## II A CRITICAL STUDY OF HEALING IN EXPERIMENTAL AND HUMAN WOUNDS UNDER ELASTIC ADHESIVE PLASTER

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In the first report<sup>1</sup> under this general title conservative and radical measures for the treatment of ulcer were evaluated according to the results obtained from each. Indications were also suggested for their use. In the course of this study it was found that ulcers which were years old and which had been refractory to many other methods of treatment healed with striking rapidity when strapped with elastic adhesive plaster—a point previously noted by A Dickson Wright, of England. Thus in this series three ulcers of an average size of 247 sq cm, all of which had failed to heal under various remedies in an average time of nine and six-tenths years, actually healed under elastic adhesive plaster in an average time of fifty-one and three-tenths days. Results such as these stimulated interest in an attempt to throw light on the mode of action of elastic adhesive plaster, a dressing which although economical and easy to apply appeared to possess the remarkable properties already described for promoting the healing of wounds. The data which I have obtained from experiments on animals and human beings are detailed in the present report<sup>1a</sup>.

During the past two years I have quantitatively checked the healing of many ulcers of various kinds and sizes and have compared their rates of healing with the calculated or ideal curves of cicatrization given by Carrel and Hartman<sup>2</sup> and Du Nouy<sup>3</sup>.

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From the Department of Surgery, Vanderbilt University

1 Douglas, Beverly Surg, Gynec & Obst **61** 458 (Oct) 1935

1a In these experiments the bandages of three firms were employed, viz, the German preparation Iomoplast, obtainable from G Kuhlman, 62 W 45th Street, New York, elastoplast, manufactured in this country and obtainable from the Duke Laboratories, Inc, Long Island City, N Y, and an English preparation prepared from the formula of A Dickson Wright and obtainable under the name of tensoplast from the Durex Products Corporation

2 Carrel, A, and Hartman, A J Exper Med **24** 429, 1916

3 du Nouy, P Lecomte J Exper Med **24** 451, 1916

to a level equal to that of the corresponding normal area. Tanning was never effective over an area of first degree burn because insufficient amounts of broken-down necrotic epithelial tissue were present to form a coagulum with the tannic acid.

The rates of evaporation from normal areas rose somewhat during the first few days, usually reaching a peak on the third or fourth day. This rise might be considered a gradual return to normal after an initial disturbance produced by the burn, or, in some cases, it might be due to the accompanying rise in general body temperature which was observed.

*Temperatures*—The surface temperatures in diverse areas of skin varied directly as the rates of evaporation (chart 1). In the tanned areas the low cutaneous temperatures that were found were probably due to the thickness and insulating properties of the tannic acid covering. In areas of first degree burns the cutaneous

*Rates of Evaporation and Surface Temperatures in Injured Areas of Patients Suffering from Accidental Burns*

Case number	4	5	6	7	8	9	10	11	12	13
<b>Second degree burns</b>										
Evaporation (mg per sq cm per min)										
Initial			0.027	0.078	0.008	0.105		0.024	0.065	0.091
Minimum after treatment with tannic acid	0.005	0.006	0.010	0.005	0.007	0.008	0.008	0.007	0.010	0.009
After recovery			0.019		0.089	0.035	0.021	0.019	0.039	0.036
Corresponding normal area	0.047	0.072	0.030		0.041	0.040	0.029	0.025		0.033
Cutaneous temperature (C)										
Initial			30.5					32.2	29.8	33.8
After treatment with tannic acid	26.4	24.8	29.0				29.8	31.2	32.4	29.9
After recovery	30.5		30.4			33.3	32.0	31.3	33.3	31.7
Corresponding normal area	29.0	27.9	32.1			32.3	32.6	32.5		31.6
<b>First degree burns</b>										
Evaporation (mg per sq cm per min)										
Initial	0.069	0.045	0.034				0.054	0.040	0.042	
After recovery	0.036		0.020				0.030	0.025	0.026	
Cutaneous temperature (C)										
Initial	32.5	31.0	29.6				34.6	32.4	31.1	
After recovery	29.8		32.3				32.0	32.1	32.2	

temperatures were higher than normal, corresponding to the higher rates of evaporation. The daily fluctuations in cutaneous temperatures did not usually correspond, however, to the daily variations in rate of evaporation.

The table shows the average values for cutaneous temperature and rate of evaporation in all but the first three cases studied. These three were not as adequately controlled as were the later experiments, and the data are therefore omitted. Of the thirteen subjects, five were children from 2 to 5 years of age.

*Sweat Glands*—The activity of sweat glands was tested in several cases. Repeated microscopic examination of the healed areas of second degree burns failed to reveal activity of the sweat glands, but the sweat glands are not actually destroyed in second degree burns.<sup>3</sup> Examination of normal areas and of healed areas of first degree burns showed active sweat glands in all cases. Richardson<sup>4</sup>

3 Pack, G. T., and Davis, A. H. Burns, Philadelphia, J. B. Lippincott Company, 1930, p. 23.

4 Richardson, H. B. The Effect of the Absence of Sweat Glands on the Elimination of Water from the Skin and Lungs, J. Biol. Chem. 67: 397, 1926.

COMPARISON OF THE RATE OF HEALING OR CICATRIZATION OF  
ULCERS UNDER ELASTIC ADHESIVE PLASTER WITH THE  
CALCULATED OR IDEAL RATE COMPUTED BY  
CARREL, HARTMAN AND DU NOUY

Nine ulcers on the legs of seven patients have been specially studied. The ages of these patients as given on the charts varied from 13 to 69 years. Tracings were made at intervals of from seven to fourteen days by the gravimetric method as described, and actual areas of unhealed granulating surface were thus calculated. The ideal rates of healing were computed by equations 1 and 2 for comparison.<sup>4a</sup>

All the ulcers, even that of A A, a 13 year old girl, were chronic and indolent. They had all been refractory to other methods of treatment. In spite of this seven of the nine actually healed more rapidly than sterile wounds of identical size would have healed according to the calculated ideal curves of healing (figs 1 and 2).

The difference in healing time noted in favor of treatment with elastic adhesive plaster probably may be explained by the fact that in the care of the wounds studied by Carrel and his associates chlorine antiseptics, such as dilute solution of sodium hypochlorite, were commonly used to attain and maintain sterility, the recognized toxicity of these substances to living tissues, even though slight, was probably sufficient to retard the healing of the wounds and thus to influence the results of calculations.

Carrel and Dehelly<sup>5</sup> compared the action of petrolatum on one portion of a sterile wound on a man's arm with the action of dilute solution of sodium hypochlorite on another portion of the same wound. At the end of four days a tracing of the wound was made, and when this was compared with the preceding tracing, it was seen that the epithelial border had progressed a little more rapidly under the petrolatum than under the solution of sodium hypochlorite. At this time both the upper and the lower part of the wound were still aseptic. Carrel and Dehelly assumed, therefore, that the solution of sodium hypochlorite had slightly retarded the healing of the wound and was slightly toxic to the organism. Elastic adhesive plaster is coated with substances which seem absolutely nontoxic to tissue. It is probable, therefore, that formulas of healing derived from wounds treated with it will prove more accurate than those already derived by Carrel and his co-workers.

Certain it is that the composite geometric curve obtained by combining the graphs of healing in the cases of F W (right leg), P H (right leg), A A, N B, S D, and H P would represent a more accurate picture of the healing of a sterile wound than would

4a Mr William W Pyle checked the computations

5 Carrel, A, and Dehelly, G. *Treatment of Infected Wounds*, New York, Paul B Hoeber, Inc, 1919, p 37

*Normal Skin*—On normal skin no coagulum formed when the skin was treated with tannic acid, and the application of tannic acid caused no appreciable change in the rate of evaporation. Attempts to form a coagulum on normal skin by first applying egg albumin were likewise unsuccessful. Hence it was not possible to ascertain the effect of tannic acid on the skin on other than injured surfaces.

#### COMMENT

The amount of fluid lost from the body owing to an accidental burn may now be calculated, for this purpose the most extreme of the burns studied is chosen. In case 9, a woman 40 years old, weighing 91 Kg and having a calculated surface area of 1.98 square meters, had a second degree burn involving one third of the surface of the body.<sup>5</sup> The initial rates of evaporation from normal, burned and tanned areas were 0.041, 0.105 and 0.008 mg per square centimeter per minute, respectively. From these figures it is calculated that the twenty-four hour loss of water would normally have been 1.29 per cent of the total body weight, but since one third of the surface of the body was losing water at a rate approximately  $2\frac{1}{2}$  times normal, the twenty-four hour loss was increased to 2.05 per cent of the total weight. After the application of tannic acid to the burned area, the twenty-four hour loss was reduced to 1.16 per cent of the total weight of the body. A woman of this weight would have an approximate volume of circulating blood of 7,000 cc and a normal rate of evaporation of 1,175 Gm in twenty-four hours. Underhill<sup>6</sup> expressed the belief that the fluid lost from burned areas is essentially blood plasma, from this it would follow that, since the burn involved one third of the surface of the body and since the rate of evaporation increased to 1,835 Gm in twenty-four hours, the blood volume might be decreased at most by the difference between the normal rate and the rate after injury, or 660 Gm.

It may be concluded, therefore, that evaporation has a negligible effect in producing dehydration after a severe burn. Even in children evaporation alone could not be important. Increased concentration of the blood, such as was found by Underhill<sup>7</sup> and others, can hardly be due ordinarily to loss of water from the body. This is confirmed by the constancy of the body weight during convalescence from burns. Hence water that leaves the blood probably remains in the body, in

5 Berkow, S. G. A Method of Estimating the Extensiveness of Lesions (Burns and Scalds) Based on Surface Area Proportions, *Arch Surg* **8** 138 (Jan.) 1924.

6 Underhill, F. P., Kapsinow, R., and Fisk, M. E. Changes in Capillary Permeability Induced by a Superficial Burn, *Am J Physiol* **95** 315, 1930.

7 Underhill, F. P., Carrington, G. L., Kapsinow, R., and Pack, G. T. Blood Concentration Changes in Extensive Superficial Burns, and Their Significance for Systemic Treatment, *Arch Int Med* **32** 31 (July) 1923. Underhill, F. P. The Significance of Anhydremia in Extensive Superficial Burns, *J A M A* **95** 852 (Sept 20) 1930.



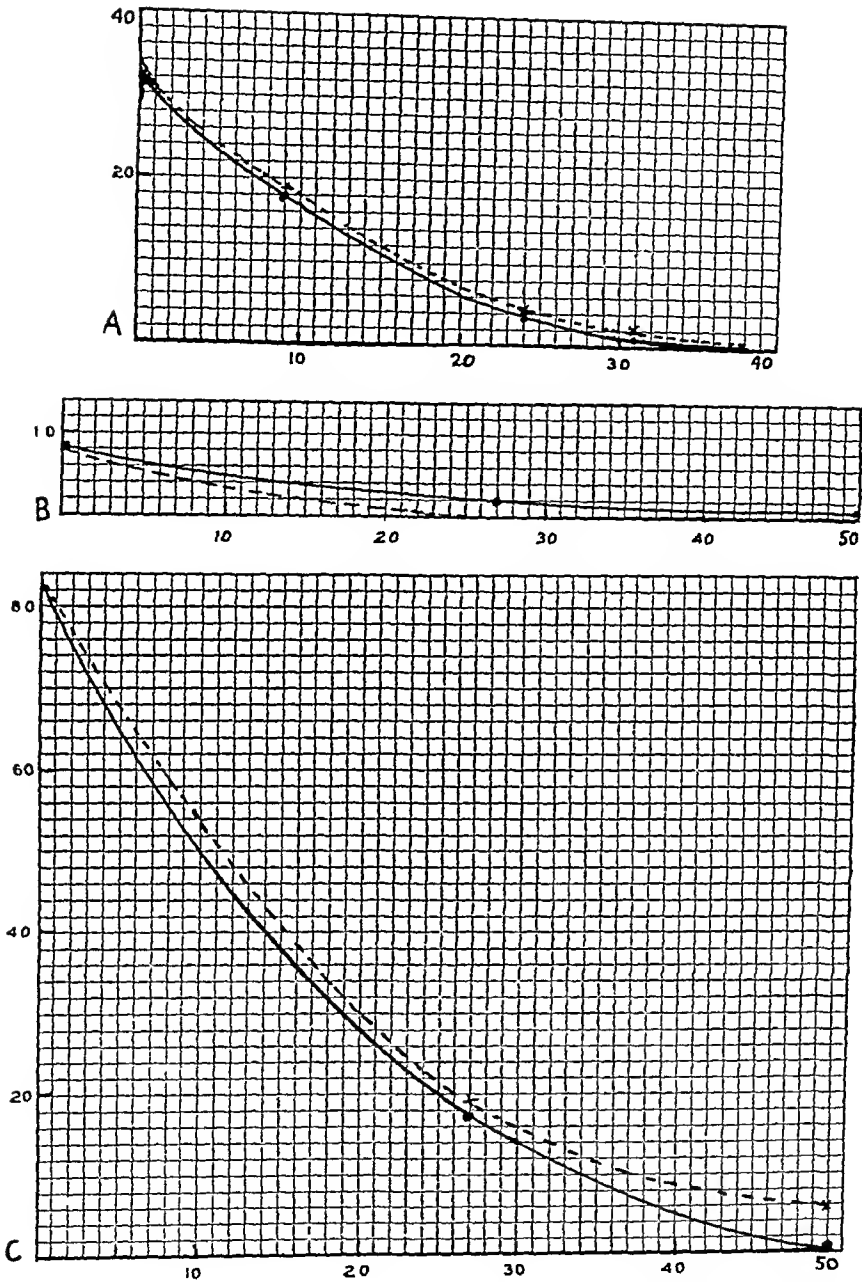


Fig 1—Curves showing healing of ulcers *A*, curve for ulcer in H P ( $i=0.038$ ), *B*, curve for ulcer on the left leg of F W ( $i=0.05$ ), *C*, curve for ulcer on the right leg of F W ( $i=0.025$ ). The solid line represents the actual curves of healing or cicatrization, the dotted lines represent the ideal curves of healing as computed by Carrel, Hartman and du Nouy. The vertical units represent areas in square centimeters, the horizontal units represent days.

## SUMMARY

Rates of evaporation were measured in thirteen cases of first degree and second degree burns, two cases of frost-bite, four cases of experimental burns produced by ultraviolet radiation and two cases in which tannic acid was applied to normal skin. In many instances corresponding cutaneous temperatures were measured.

It was found that the rates of evaporation from areas of first degree and second degree burns increased. Tannic acid formed (in second degree burns) a hard covering and prevented evaporation. In areas of first degree burns evaporation remained high. Evaporation from corresponding normal areas often increased somewhat for the first few days and then gradually returned to normal.

Cutaneous temperatures in burned as well as in normal areas were temporarily increased, corresponding in general to the rates of evaporation.

The failure of the rates of evaporation in areas of second degree burns to return completely to the normal level was correlated with the incomplete function of sweat glands, since no evidence of their activity could be demonstrated.

The changes in rate of evaporation and in cutaneous temperature in the cases of frost-bite and in the burns caused by ultraviolet radiation were essentially those of second degree and first degree burns, respectively. Tannic acid did not form a coagulum on areas of first degree burns, on irradiated skin or on normal skin.

When rates of evaporation were calculated for the whole body over a twenty-four hour period, it was ascertained that no significant changes in the weight of the body and no important losses in the total amount of fluid would be expected to result from evaporation alone.

Several aspects of the local action of elastic adhesive plaster on the wound proper appear to be responsible for the remarkable rapidity with which healing is accomplished

In the first place it provides moist healing conditions without permitting the formation of a dead space. Plasma and pus when excessive may filter out of the minute spaces between the threads of waterproofed cloth. It is therefore semipermeable. In 1913 Halsted<sup>6</sup> pointed out the advantages of maintaining the moisture of the edges of the wound during healing in the following words

A moist scab, so-called, is better than a dry one. The surgeon has many opportunities to convince himself of this. When he has occasion to extract a toe-nail let him cover one-third of the raw surface with protective [gutta-percha tissue] and allow the remainder to heal under the dry scab. The patient may have pain in the digit soon after the dry scab is well formed, and the surgeon will perhaps observe that the soft parts about the nail-bed on the side of the dry scab are inflamed. On covering the entire surface of the granulating wound with gutta-percha tissue the pain will be relieved and the inflammation subside.

The dry scab imprisons secretion which in turn gives rise to tension, and the tension impairs the vitality of the tissues under and at the border of the dry scab to an extent sufficient to place them at a disadvantage with the micro-organisms and to compel absorption of the toxins.

Elastic adhesive plaster does not imprison secretions to any appreciable extent, for the exudate comes out through the plaster as well as around its edges. It does, however, provide moist healing conditions—"a moist scab, so-called"—the advantages of which Halsted so well emphasizes in this description. That the irritation and pain so commonly experienced with a dry dressing are promptly relieved by elastic adhesive plaster is attested by the repeated statements of patients who have had it applied to their ulcers.

Another action of a dressing such as this which provides moist conditions was not specifically mentioned by Halsted, namely, that by protecting the surface from recontamination or reinfection by outside organisms it permits the blood to build up at the wound antibodies definitely specific for the particular organisms present at first. This is an aid to rapid sterilization and thus to rapid healing.

One disadvantage of a dressing which fails to maintain moist conditions on the surface of the wound is that drying destroys the leukocytes and must also destroy antibodies. This was emphasized by A. Dickson Wright in a recent article.<sup>7</sup> Thus the forces of resistance of the body to micro-organisms are broken down by a drying of secretions

<sup>6</sup> Halsted, W. S. Ligature and Suture Material, *J. A. M. A.* 60:1119 (April 12) 1913.

<sup>7</sup> Wright, A. Dickson. *Brit. M. J.* 2:561 (Sept. 26) 1931.

It will be recalled that by determining the surface area of sterile wounds by means of a planimeter these authors were able to derive simple and exact mathematical equations expressing the rate of healing. From these equations it is easy to predict the amount of healing which would take place in a given period of days for a sterile wound.

First it is necessary to obtain an index of cicatrization, <sup>1</sup> This is calculated by equation (1)

$$(1) \frac{\frac{S-S'}{S}}{t + \sqrt{T}} = 1$$

Then the area of the wound after a given lapse of time may be calculated by a second equation, equation (2)

$$(2) S'' = S' [1 - i(t' + \sqrt{T+t})]$$

Du Nouy explained the symbols as follows

*S* represents the area of the wound at the beginning of the experiment

*S'* represents the area of the wound *t* days later, at the time of the second observation

*t* represents the time elapsed between the first two observations, *S* and *S'*, in days

*T* represents the age of the wound from the time of the first observation *S*. Therefore in the formula (1) *T* = *t*, and practically *t* = *t'*

*t'* represents the time between the last observation *S'* and the time of the theoretical surface *S''* of the wound

*i* is a constant coefficient characterizing each wound

#### APPLICATION OF THE EQUATIONS TO THE PRESENT SERIES

At each visit excess secretions were blotted from the ulcers to be studied. Cellophane wound on cardboard spools and sterilized in an autoclave was unwound with sterile instruments and laid over the ulcer. The epithelial edge plainly visible through this was traced in a dotted line in ink with a fine pointed pen. The cellophane bearing the pattern was removed and stuck on a square of glass while the secretions were still moist on its under-surface. The hospital record sheet was then laid over the cellophane and the exact pattern traced on the record as silhouetted through the cellophane. Later this pattern was transferred by means of carbon paper to a sheet of standard bond paper of known weight and size. It was finally cut out of the bond paper and weighed. A simple division gave the exact area in square centimeters, and this in reality represented the actual area of the wound on the date on which the tracing was made. The details of this method for calculating the size of wounds are given in a previous article <sup>4</sup>

<sup>4</sup> Douglas, B. Ann Surg 73 673, 1921

healing process. How does it do it? The essential rôle that moderate pressure plays in promoting "takes" in whole thickness skin grafts by insuring contact and lessening inflammation is well known. I am certain that a similar rôle is played by pressure in the healing of ulcers without grafts. First, if proud flesh, or exuberant granulation tissue, is present its further formation is checked and that already formed is pressed back by the constant elastic pressure. This rapidly produces a granulating surface level with the epithelium and favors the latter's rapid advance over it. Conversely, the epithelial edge surrounding a depressed wound will be gradually pressed down to the lower level of the granulating surface.

By accident in August 1932 I dressed a patient on whose leg an elastic adhesive bandage had been improperly applied. The turns of the bandage had been made to overlap each other too little. The leg was

TABLE 1—*Comparison of the Effect of Saturated Solution of Boric Acid with That of Elastic Adhesive Plaster on Bacteria and Healing of Ulcers of E W*

Date	Ulcer a *		Ulcer b †	
	Number of Colonies on Culture	Size	Size	Culture
9/11	Innumerable	Small	Large	Infinity
9/16	Innumerable	Small	Large	5 colonies
9/20	Innumerable		Small	Sterile
10/ 2	Sterile	Small	Small	
10/ 4		Small	Healed	
10/21		Healed		

\* Ulcer a was treated with a solution of boric acid

† Ulcer b was treated with elastic adhesive plaster

therefore found to have been pressed too hard in certain places, while little if any pressure had been exerted in others. Multiple ulceration was present. When the bandage was removed an interesting and instructive phenomenon was seen. Wherever the turns of the bandage had pressed firmly against the tissues the ulcers were healed. On the contrary, wherever the turns had been too loose the granulations were exuberant, and epithelium had not grown over. In some places these two conditions were seen side by side in the two halves of a single ulcer. A photograph of the wound shows this clearly.<sup>8</sup> The rôle of the elastic adhesive bandage in producing elastic pressure to hold down granulations was thus excellently demonstrated.

<sup>8</sup> Since this report was submitted I have read with interest an article by E. D. Twyman published in the *Journal of the Missouri State Medical Association* (191 [June] 1922), entitled "Epithelial Proliferation, Differential Pressure as an Aid in the Growth of Epithelium on a Denuded Surface." Twyman expressed the belief that epithelium proliferates readily when it is subjected to a degree of pressure which restrains the growth of granulations. The report contains a photograph of a wound showing "a bar of epithelium grown across from side to side

the composite graph of Carrel and Hartman's curves. It is noted that in the latter graph the curve is not as steep as, and reaches the abscissa at a later date than, in the graph for healing of wounds in treatment of which no antiseptic was used (figs 1 and 2).

It is believed that the facts that healing of these old ulcers of the leg is so rapid under elastic adhesive plaster, a chemically inactive dressing the properties of which are admittedly almost entirely physical and that dilute solution of sodium hypochlorite is admittedly slightly toxic to tissues both indicate that progress in the development of therapeutic measures to promote or aid healing of wounds will be made in the future along physical rather than along chemical lines.

One point is believed to be of great importance namely that as definitely shown by Carrel and Hartman<sup>2</sup> contraction is the more important factor in healing of wounds and that epidermization completes the work of contraction in healing. It is likely that with elastic adhesive plaster the constant pull inward (at least in one dimension or direction) tends to promote contraction in tissues which have been prevented from exercising this important function in healing by such factors as edema and excessive deposits of scar tissue.

In any event it seems astounding that these large, chronic ulcers should have healed more rapidly than if they had been fresh sterile wounds.

Two ulcers did not heal as calculated ideal curves indicated that they should have healed. One of these had been present in a man of 39 for ten years and was surrounded by a dense and deep scar. Du Nouy's formula indicated that it should have been healed on the twenty-third day. A tracing on the twenty-seventh day showed that it measured 4 sq. cm., and on the fiftieth day it still measured 0.33 sq. cm., after that I did not see the patient (fig 1 B). Meanwhile a much larger ulcer on the other leg healed more rapidly than the ideal curve indicated that it should, showing that some local factor which was not discovered caused the first ulcer to heal so slowly (fig 1 C).

The other patient, a Negro aged 58, had a nonspecific elephantiasis from an old thrombophlebitis and two ulcers which were of twenty years' duration. One ulcer healed under elastic plaster more rapidly than the curve of ideal healing indicated that it should (fig 2 C). The other ulcer rapidly diminished in size and measured only 1.5 cm. in twenty-five days but a small deep area remained unhealed under this treatment until fourteen months later, when strapping with a pad over the plaster was successful in accomplishing complete cicatrization (fig 2 E). I am certain now that the ulcer would have healed more promptly if the application of the pad had been resorted to sooner.

latter days of healing it is seen that the area of the scar actually enlarged, which means that since contraction was lacking, epidermization became more rapid and compensated for the dilatation of the cicatrix.

The second chart, or figure 5, represents the curve of healing of a shell wound of the external part of the leg in a patient 39 years of age. It is seen to be quite different from that in figure 4. Thus, between January 3 and 15 contraction alone was largely responsible for healing. Between January 15 and 19, since the upper curve remains horizontal, the downward deflection of the lower indicates that epidermization was responsible for healing. After this both processes took part in the healing of the wound though epidermization assumed the major role.

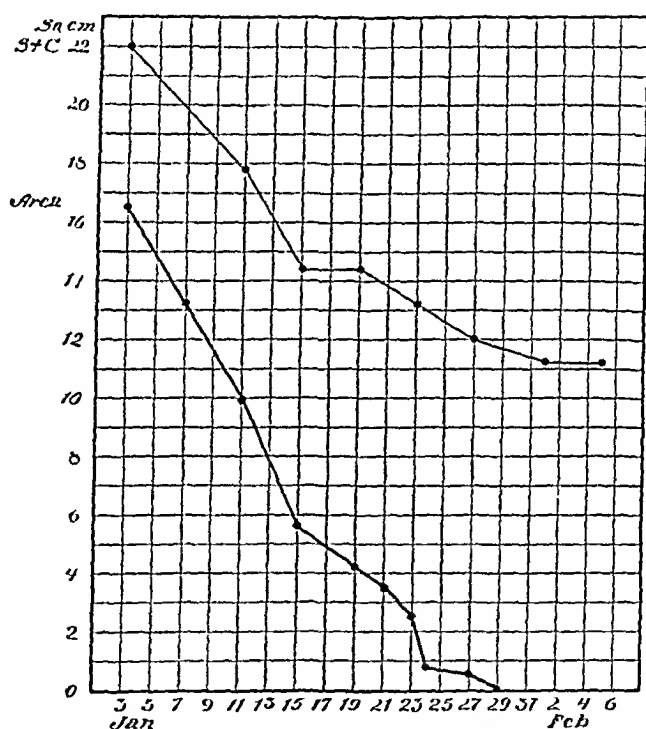


Fig 5—Curve of healing of a shell wound of the external part of the leg in a patient 39 years of age. (The graph is figure 21 of the article by Carrel and Hartman<sup>2</sup>)

From these curves, then it can be seen that two processes—contraction and epidermization, contribute to healing of wounds in varying degrees, according to the particular wound. Carrel and Hartman stated that contraction, as a process, is dependent on contraction of granulation tissue and on the opposite action of the tissues surrounding the wound. According to them, the resistance of the skin surrounding the wound is slight in narrow wounds, and in larger defects the wound contracts until the elasticity of the surrounding skin prevents a greater reduction of its size.

## MODE OF ACTION

The general action of elastic adhesive plaster in compressing dilated veins and thus improving the nutrition of the tissues is like that of the elastic stocking and other similar devices. Owing, however, to its

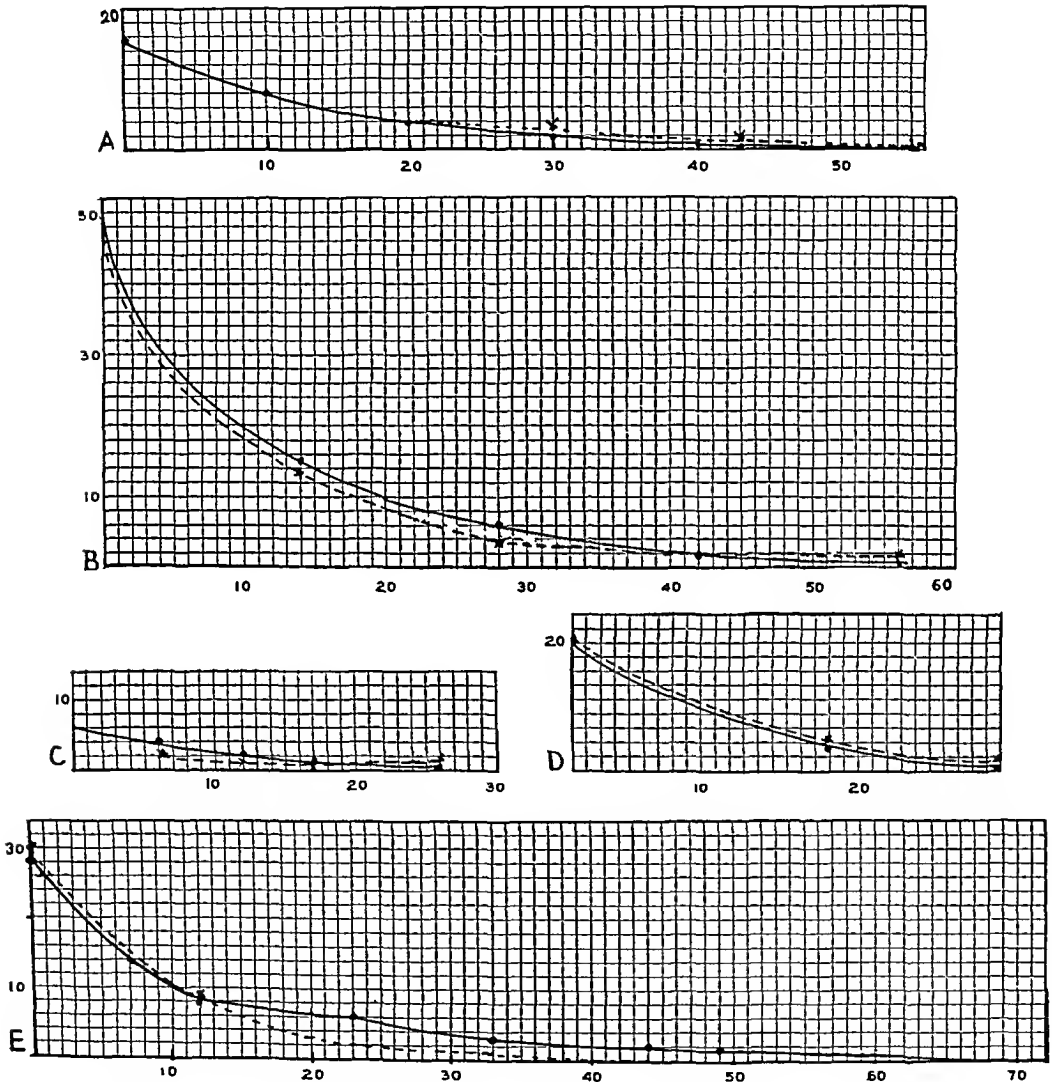


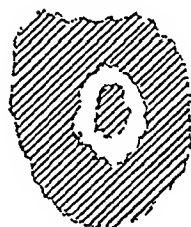
Fig 2—Curves showing healing of ulcers *A*, curve for ulcer in S D ( $i=0.032$ ), *B*, curve for ulcer in N B ( $i=0.039$ ), *C*, curve for ulcer on the right leg of P H ( $i=0.025$ ), *D*, curve for ulcer in A A ( $i=0.33$ ), *E*, curve for ulcer on the left leg of P H ( $i=0.19$ ). The vertical units represent areas in square centimeters, the horizontal units represent days.

adhesive coating it holds securely to the leg and maintains a more even and constant pressure on varicosities until the latter can be treated by curative measures.



As the wound healed, therefore, the vertical diameters were reduced almost exactly proportionately to the horizontal diameters, the ratio  $49/42$  being approximately equal to  $27/25$

## EXPERIMENT A



1 18-29



1 18-29



1 21-29



1-23-29



1-25-29



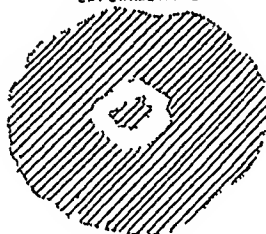
1-28-29



## EXPERIMENT B



1-23-34



1-23-34



1-30-34



2-6-34



2-13-34



2-20-34

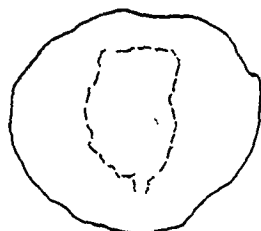


Fig 6—Diagrams showing healing of a ring of skin on a granulating surface (experiment A) and healing of a ring of skin under elastic adhesive plaster (experiment B)

EXPERIMENT B—On a dog anesthetized with ether a wound similar to that of the dog in experiment A was made by excision of skin from the abdomen. In this experiment, however, the outer outline was made larger and the greatest

Elastic adhesive plaster obviates this by keeping the wound moist at all times without permitting the formation of an appreciable dead space. Its value from this standpoint is obvious.

Bacteriologic studies bearing on this point are not yet complete, but I report the following case, which was studied fully by Dr. Robert Schrek and me.

E. W., a college girl aged 24, scratched her legs while walking through briars on about Aug. 3, 1933. Ulcers developed at the sites of the scratches, and on admission to the hospital on August 9 there were sixteen ulcers on her legs. The two largest were chosen for special study. By reference to the photographs the method of procedure and the results may easily be followed. For purposes of clarity hereafter the ulcer chosen for observation on the right leg will be designated as *a* and the one at a corresponding level on the left leg as *b*.

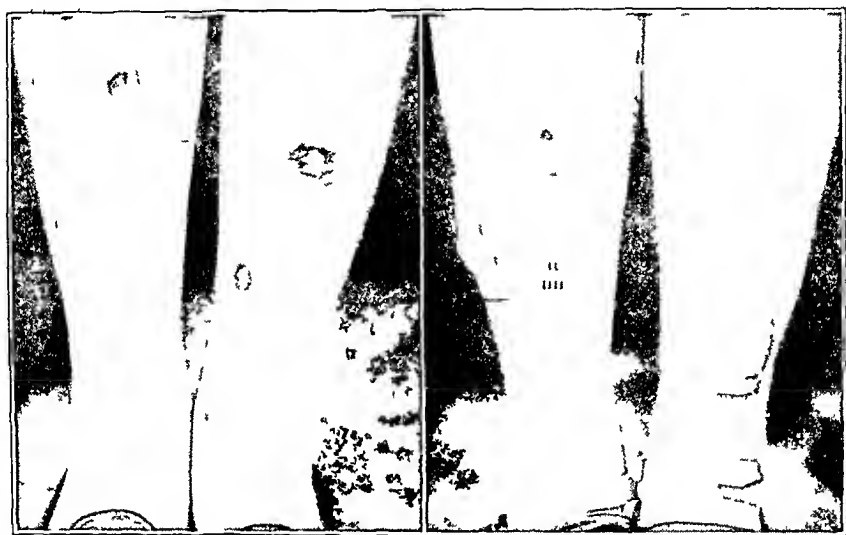


Fig. 3—Bilateral ulcers on the legs of E. W. At left, condition at start of treatment (September 11), at right, ulcer, *a*, on the right leg, which was treated with a solution of boric acid, is still open, ulcer, *b*, on the left leg, which was treated with elastic adhesive plaster, is healed. See also table 2.

From figure 3 it is readily seen that on September 11 *b* was almost twice as large as *a*. The subsequent treatment and results are shown in table 1.

Thus, *b*, a larger ulcer than *a*, when treated by elastic adhesive plaster became sterile in nine days (or twelve days earlier than *a*) and healed seventeen days sooner than *a* which was treated by gauze packs moistened with warm saturated solution of boric acid.

Another property of elastic adhesive plaster which I consider valuable and which I am therefore studying rather intensively is its persistent elastic pressure on the wound—an action which for want of a better term I call a "gloving action." I have been forced recently to conclude that this plays a major rôle in the actual speeding up of the

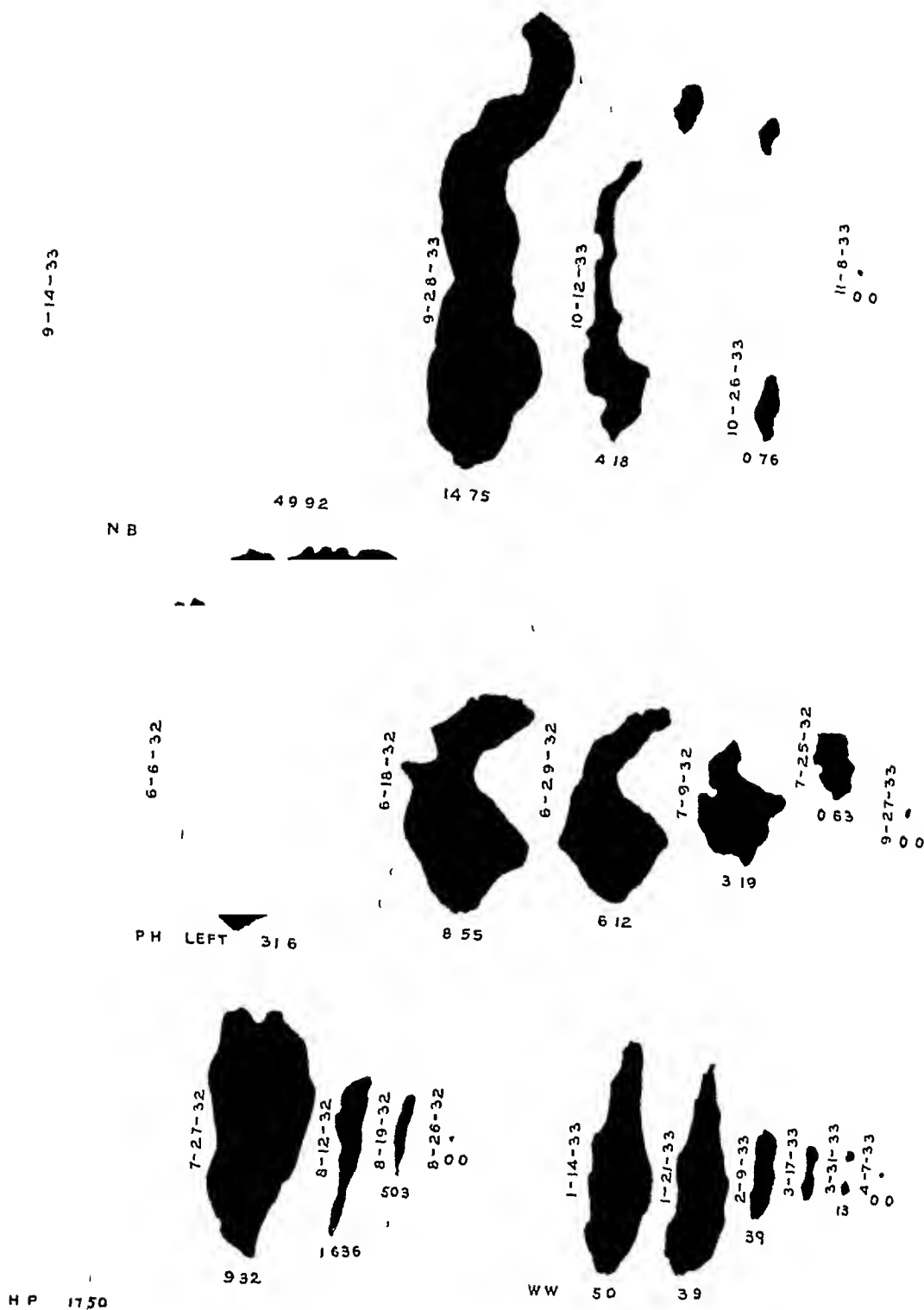


Fig 7—Cut-outs showing progressive healing of human ulcers The horizontal numbers indicate areas of wounds in square centimeters, the vertical numbers show the dates

## CONTRACTION OF TISSUES

The function that contraction plays in healing, as emphasized by Carrel and Hartman, has already been mentioned. It is obvious that the concentric pull of elastic adhesive tape must greatly favor this and must therefore be important in promoting healing of wounds.

In eight cases they studied the parts that contraction and epidermization each play in the healing process. For the purpose of discussion two of their charts are reproduced.<sup>2</sup>

The first of these, figure 4, represents the graphic curve of healing of a wound of the upper clavicular region. The lower curve represents the total surface area of the unhealed or granulating portion of the

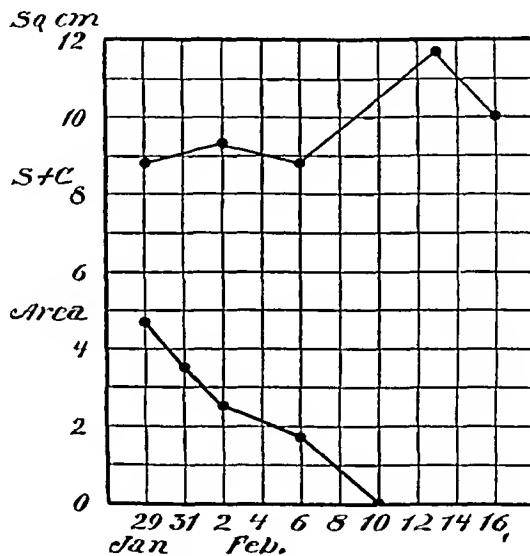


Fig 4—Graphic curves of healing of a wound of the upper clavicular region. The graph is figure 19 of the article by Carrel and Hartman.<sup>2</sup>

wound. The upper curve represents this plus the area of the scar already formed. It was obtained by tracing the outer border of the scar or cicatrix on cellophane and determining the area included by the use of a planimeter. It is seen, as Carrel and Hartman pointed out, that the upper curve remains horizontal for a while and afterward inclines upward. Cicatrization or healing in this case was therefore due entirely to epidermization and not to contraction. During the

by strapping across it" with ordinary nonelastic adhesive plaster. His observations were well made, and I agree with him as to the value of ordinary adhesive plaster. This work should go far toward substantiating the view expressed first by Morison and then by Carl Beck, who advocated treatment of superficial wounds by means of strapping with adhesive plaster. It is in direct line with my observations on the healing of wounds under elastic adhesive plaster.

transversely so as to produce a pressure inward toward the center of the leg of about 2 to 3 pounds (0.9 to 1.3 Kg.) per square inch. Tracings were then made at regular intervals as the ulcers healed.

In order that the progressive decrease in the areas of the wound might be visualized, cut-outs of their outlines placed over black paper were employed. A few of these are shown in figures 7 and 8. These cut-outs show quite a uniform tendency for the transverse or horizontal

TABLE 3 (*Experiment B*)—*Linear Measurement of Greatest Diameters of Wound in Centimeters*

Date	1/23	1/30	2/6
Vertical measurement	5.3	4.8	4.6
Horizontal measurement	6.2	3.9	3.6

TABLE 4 (*Experiment B*)—*Linear Measurement of Greatest Diameter of Cicatrix in Centimeters*

Date	1/23	2/13	3/20
Vertical measurement	5.3	3.3	3.3
Horizontal measurement	6.2	2.2	2.3

TABLE 5—*Comparative Decrease in Maximum Vertical Dimension (V) and Maximum Horizontal Dimension (H) of Ulcers in Centimeters (Elastic Adhesive Plaster Applied Transversely to Long Axes of Ulcers)*

Case	V <sup>1</sup>	V <sup>2</sup>	H <sup>1</sup>	H <sup>2</sup>
H. P. (25)*	6.4	3.5	3.7	0.7
W. W. (26)	5.2	2.1	1.4	0.4
S. D. (30)	5.8	2.9	3.2	0.9
P. H. (33)	3.2	1.7	1.7	0.7
N. B. (14)	12.4	9.6	7.3	2.5
Totals	33.0	19.8	17.3	5.2

\* The figures in parentheses denote intervals in days between measurements in each case.

dimension of the ulcer to decrease proportionately more rapidly than the vertical. In other words, the wounds in general assume a long narrow shape, so that the edges lying lengthwise of the extremity are brought close together before healing takes place.

From table 5 it is evident that under the effect of transverse traction by elastic adhesive strapping the widths of all the ulcers decreased much more rapidly than their heights. By figuring out the proportions, the transverse dimension is found to decrease 1.9 times, or almost twice, as rapidly as the vertical.

These facts may easily be verified by considering the pulling apart or retraction of edges of skin which occurs when a circle of skin is excised from a dog's abdomen. The outline of the pattern (fig 6 experiment A) along which the circular incision was made measured 5.2 cm in its transverse diameter, but after the central skin was excised it measured 6.3 cm. Every surgeon is well acquainted with the gaping of the edges of a wound which occurs when a simple line incision is made and knows how large an area from which a full thickness graft is cut may become by retraction of edges. Traction by adhesive tape is often used in the surgical treatment of wounds resulting from accidents in place of sutures to decrease the size of skin defects. It is probable that elastic adhesive plaster may accomplish similar results more gradually in older wounds by slowly overcoming the outward pull of the surrounding skin.

In certain old ulcers a share of the failure to heal or tardiness in healing which occurs at times may be due to the fact that granulations are unhealthy and fail to contract. It is wholly logical that elastic adhesive plaster may supply the force to contract and heal which is lacking in such cases.

Knowing these facts, I decided to investigate the exact effect of the constant mechanical tension of elastic adhesive plaster in one dimension toward the center of the wound on the process of contraction.

#### EXPERIMENTAL EVIDENCE THAT ELASTIC ADHESIVE STRAPPING FAVORS HEALING THROUGH CONTRACTION

**EXPERIMENT A**—Three oval outlines were marked off on the abdomen of a dog after it had been shaved. With the animal under ether anesthesia the skin was excised between the two outer outlines and inside the inner one, thus leaving a circular band or 'doughnut' of skin isolated on a raw surface which was to serve for a different study. Tracings on cellophane of the epithelial edge of the outermost circle were made regularly every two days as the edge grew inward toward the center. Tracings on the same cellophane were made of the outline of the circle of skin as the edges of the latter grew inward and outward, respectively. At each dressing the wound was covered with dry sterile gauze strapped on with adhesive plaster.

The progress of healing is shown by the reduced drawings (fig 6, experiment A). In the last tracing the heavier outer ring represents the outline of the wound at the start of the experiment. The inner dotted lines represent the degree of advancement of the healing edges twelve days later.

From these drawings it is seen that the shape of the wound, an oval with the greatest dimension vertically placed, remained much the same during healing when an ordinary type of dressings was used. Measurements showing this to be true are given in table 2.

long and narrow during healing, or, in other words, in general they retain their original shapes. These shapes, incidentally, have been shown to be the ones best adapted for the attainment of rapid healing.

It is to be noted in this connection that while the lengths of the narrow wounds are not sufficiently decreased to alter completely the shapes of the wounds, nevertheless they show decreases which are marked when considered relative to the changes in wounds not treated with elastic plaster. If healing had not supervened too early, their shapes would probably have been altered. The case of Q. W. corroborates this, since just before healing the wound assumed an almost circular shape, with a vertical diameter of 0.55 cm. and a horizontal diameter of 0.5 cm.

The data on experimental wounds and on wounds in human beings which we have presented show that elastic adhesive plaster favors contraction in one axis of the wound and through this action greatly favors the healing process.

One more question seems pertinent to the discussion. Since it is known that a surface wound such as an ulcer has two dimensions and elastic adhesive plaster can contract in only one of these, why would not more rapid healing be obtained by using a material uniformly elastic in all directions, such as finely perforated dental rubber-dam impregnated with the same kind of plaster? Such a plaster would shrink the wound inward in all directions. In answer, I may say that I have already used strips of elastic adhesive strapping vertically as well as longitudinally simultaneously over wounds by stretching a strip up the side of the leg and covering it with the usual spiral turns. The effect seems to be better than that produced by using the spiral turns alone. It is readily seen, however, that since the cloth is not elastic in the direction of its width this nonelasticity must necessarily impede the pull inward in this direction of the overlying cloth.<sup>9</sup>

#### SUMMARY AND CONCLUSIONS

In a previous report, prompt healing under elastic adhesive plaster was reported in 96.7 per cent of chronic ulcers, most of which had been refractory to other nonoperative forms of treatment.

A closer study of a typical group of ulcers by quantitative methods shows that (a) The healing rate of most chronic ulcers treated by elastic adhesive strapping is more rapid than the ideal rate of healing for recent wounds kept sterile by dilute solution of sodium hypochlorite.

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<sup>9</sup> Since this article was submitted I have constructed a semipermeable elastic adhesive cloth which is uniformly elastic in all directions. This has been named *equiplast*. The effect which it has already produced on experimental and human wounds will be made the subject of a further report.

diameter of the oval was placed horizontally instead of vertically. Similar tracings were made throughout, but in addition the outline of the cicatrix was traced so as to determine how much contraction of the scar, if any, occurred. Instead of the ordinary dry gauze dressings used in experiment A, elastic adhesive plaster was stretched firmly in a horizontal direction across the wound and was replaced at each tracing. Figure 6 (experiment B) shows the progressive changes in outline during healing. The heavier outer ring in the last tracing represents the outline of the wound at the start. The inner heavier dotted outline represents the advancement of the edge after fourteen days of healing. The innermost circle shows the final shape and size of the cicatrix.

It may be noted that the shape of the wound was changed by elastic adhesive strapping from a horizontal oval to a vertical oval.

*Results*—The results as given in tables 3 and 4 are self-explanatory.

Thus it is seen that the shape of the wound was changed during healing in such a manner that the horizontal diameter, which was originally greater, became smaller than the vertical. The original fraction representing the relation of the vertical to the horizontal dimension changed from  $5\frac{3}{6}2$  to  $4\frac{6}{3}6$ .

TABLE 2 (*Experiment A*)—*Linear Measurement of Greatest Diameters of the Wound in Centimeters*

Date	1/16	1/18	1/21	1/23	1/25	1/28
Vertical measurement	4.9	4.5	3.6	3.7	3.1	2.7
Horizontal measurement	4.2	4.2	3.9	3.4	3.4	2.5

When one turns attention to the cicatrix or scar, it is found that a similar condition exists. The original fraction representing the relation of the vertical to the horizontal dimension changed from  $5\frac{3}{6}2$  to  $3\frac{3}{2}3$ . The greatest decrease in the size of both the granulating surface and the scar in experiment B is seen to occur in the horizontal dimension, in which the inward pull of the elastic adhesive bandage was exerted. Since there was no corresponding change in either diameter of the wound in experiment A, which was treated without elastic adhesive bandage, it is concluded that the latter is responsible for the diminution in size or the contraction produced. Also, since it was found that the healing was much more rapid in the wound treated with elastic adhesive bandage, it was concluded that the contraction which was shown to be present must play a favorable rôle in healing.

*Evidence from Human Wounds*—I have made similar studies based on human wounds of the role of contraction or shrinkage of wounds due to the pull inward of elastic adhesive strapping which is applied spirally about the lower extremity. The patients in each case had one or more ulcers of the leg. The elastic adhesive bandages were applied



# SHOCK THE MECHANISM OF DEATH FOLLOWING INTESTINAL OBSTRUCTION

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AND  
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The mechanism by which death results from intestinal obstruction remains a much debated question. The literature on this subject is voluminous, and extensive experimentation has led to dissension rather than to agreement. The reports are characterized by general similarity in the essential results of experimentation and by diversity of interpretation. No attempt will be made here to analyze these reports. The analysis by Cooper<sup>1</sup> considered 161 articles, and reflected the divergent views of the authors. He reviewed the evidence and interpretations and closed his summary with the unanswered question "What is the cause of death in high intestinal obstruction?"

In studies on shock of various origin in man and on experimental shock, we are struck by the similarity between that condition and the phenomena resulting from intestinal obstruction. When shock is induced in dogs without trauma and without the complicating factor of deep narcosis, a characteristic group of symptoms is produced. The animal becomes inactive and listless and refuses food. There are muscular tremors, vomiting, salivation and, in the later stages, the passage of fluid stools, which frequently contain blood and mucus. The pulse becomes rapid, the blood pressure falls, the temperature becomes subnormal or sometimes increased and the respirations are slow and deep. The blood becomes markedly concentrated, the non-protein nitrogen content increases and the coagulability decreases. The urine becomes scanty and concentrated. Frequently it contains blood and albumin. Lethargy or coma and evidence of circulatory failure precede death.

This syndrome as described may be produced by introducing fresh finely chopped dog muscle into the peritoneal cavity, by the intravenous injection of peptone, of watery extracts of various tissues, of histamine, mercury bichloride or various other drugs or of sterile suspensions of bacteria or bacterial products and by other means.

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This work was aided by the Martin Research Fund

From the Department of Pathology, Jefferson Medical College

1 Cooper, H S F Cause of Death in High Obstruction, Arch Surg

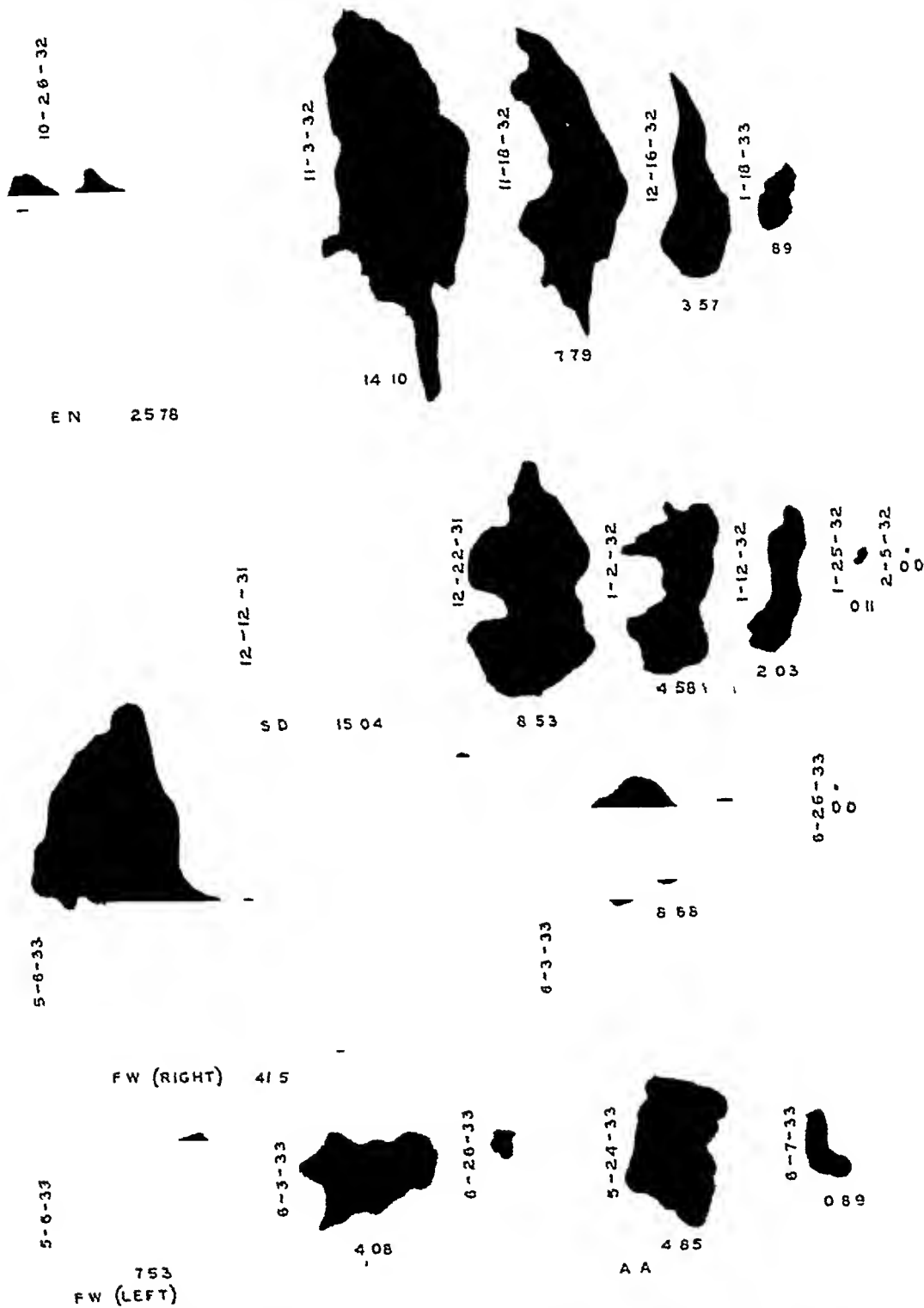


Fig 8—Cut-outs showing progressive healing of human ulcers. The horizontal numbers indicate areas of wounds in square centimeters; the vertical numbers show the dates.

The peritoneal surfaces of the bowels were rose-red or bluish red. The mucosae were dark red and contained numerous hemorrhagic flecks. Similar minute hemorrhages were present in the surfaces of the liver, spleen and kidneys. Blood-tinged fluid was present in the serous cavities. The lungs were deep red and contained numerous ecchymoses in their substance and also in the pleura. Blood flowed freely from the cut surfaces of the organs. The outstanding microscopic features were distention and engorgement of the minute vessels in all the tissues. There were numerous capillary hemorrhages in the substance of the organs especially in the lungs, liver and kidneys. Heubner concluded that circulatory failure resulted from the widespread dilatation of the capillaries and venules. The animals had bled to death into their own capillaries as he expressed it.

Dale and Laidlaw<sup>5</sup> noted similar circulatory changes in shock following injections of histamine. An increase in the concentration of hemoglobin and red cells of 40 per cent was an associated feature.

Observations on congestion, edema, capillary hemorrhages and hemoconcentration (increase in the concentration of hemoglobin and red cells) were recorded by many authors (Hooker,<sup>6</sup> Gasser and his associates,<sup>7</sup> Keith,<sup>8</sup> Bayliss,<sup>9</sup> Cannon and his co-workers,<sup>10</sup> Whipple and his co-workers<sup>11</sup>) in studies on traumatic shock. In the records of postmortem examinations after shock from battle wounds, marked congestion and edema of the viscera, effusions of fluid into serous cavities and capillary hemorrhages in mucous and serous surfaces were noted.

5 Dale, H. H., and Laidlaw, P. P. *J. Physiol.* **52**: 110 and 355, 1919.

6 Hooker, D. R. *Am. J. Physiol.* **54**: 30, 1920.

7 Gasser, H. S., Erlanger, J., and Meek, W. J. *Am. J. Physiol.* **49**: 90 and 151, 1919; **50**: 31, 1919.

8 Keith, N. M. *Blood Volume in Wound Shock*, in Reports of the Special Investigation Committee on Surgical Shock and Allied Conditions. VIII. Traumatic Toxaemia as a Factor in Shock, Medical Research Committee, Special Report Series, no. 26, London, His Majesty's Stationery Office, 1919, p. 36.

9 Bayliss, W. M. *Observations on the Results of Muscle Injury and Their Treatment*, in Reports of the Special Investigation Committee on Surgical Shock and Allied Conditions. VIII. Traumatic Toxaemia as a Factor in Shock, Medical Research Committee, Special Report Series, no. 26, London, His Majesty's Stationery Office, 1919, p. 23.

10 Cannon, W. B. *Some Characteristics of Shock Induced by Tissue Injury*, in Reports of the Special Investigation Committee on Surgical Shock and Allied Conditions. VIII. Traumatic Toxaemia as a Factor in Shock, Medical Research Committee, Special Report Series, no. 26, London, His Majesty's Stationery Office, 1919, p. 27. *Traumatic Shock*, New York, D. Appleton & Company, 1923. Cannon, W. B., Fraser, J., and Hooper, A. N. *Medical Research Committee Special Report Series*, no. 25, 1919, p. 72.

11 Whipple, G. H., Smith, H. P., and Belt, A. E. *Am. J. Physiol.* **52**: 72, 1920.

In the case of N B linear measurements of the outline of the scar or cicatrix gave the values shown in table 6. These values indicate that healing in this case proceeded by means of both contraction and epidermization but that the former must have paved the way for the latter by helping to render the wound a long narrow one. Since the contraction is seen to have occurred almost totally in one dimension, viz, the horizontal, it seems certain that the transverse concentric pull inward of the elastic adhesive plaster must here as in all the cases previously referred to, have exerted a favorable influence on the factor of contraction.

Since the elastic adhesive plaster used in these studies exerts a force in only one direction, the question logically arises: What would

TABLE 6—*Linear Measurements of Greatest Diameter of Cicatrix in Centimeters (N B)*

Date	9/14	9/28	10/12	12/13
Horizontal measurement	7.3	5.4	4.6	4.3
Vertical measurement	12.4	11.8	12.2	12.0

TABLE 7—*Comparative Decreases in Maximum Vertical Dimension (V) and Maximum Horizontal Dimension (H) of Ulcers in Centimeters (Elastic Adhesive Plaster Applied Lengthwise to Long Axis of Ulcers)*

Case	V <sup>1</sup>	V <sup>2</sup>	V <sup>3</sup>	H <sup>1</sup>	H <sup>2</sup>	H <sup>3</sup>
F W	3.9	2.5	0 (healed)	10.5	5.4	0
Q W	2.3	1.7	0.55	3.9	2.9	0.5
B A	1.1	0.5	0.35	1.7	1.1	0.9
Totals	7.3	4.7	0.9	16.1	9.4	1.4

be the effect of applying the plaster so that its pull is inward in the direction of the long dimension or axis of a wound instead of in the short axis? In other words, what would be the effect of applying the plaster so that its pull centrally would be exerted lengthwise of a long narrow wound? Unfortunately most patients available for study had ulcers of the legs, and these were narrower in the long axis of the leg than they were in the short transverse axis, or the direction in which the elastic adhesive plaster was stretched to encircle the leg.

The opposite was true in three cases, however. In these the ulcers were long in the transverse axis of the leg and comparatively narrow. The elastic pull of the adhesive plaster was exerted inward along their long axes.

Table 7 shows that in spite of the pull of the elastic adhesive plaster being inward along the lengths of the ulcers the latter remain relatively

the systemic demand. In a few instances we have found the spleen relaxed, atonic and engorged, but usually it is contracted, dry and bloodless.

In the reported experiments on intestinal obstruction the details of postmortem observations are fragmentary. Yet the records agree in the frequent mention of marked congestion and capillary hemorrhages in the gastro-intestinal mucosae in parts not involved by the obstruction. The capillaries and venules along the mesenteric attachment are engorged and distended, and there is marked congestion of other viscera, especially of the liver and kidneys. The blood clots slowly and appears concentrated. Marked congestion of the lungs and of the mucosa of the respiratory tract are reported frequently.

The decrease in blood chlorides accompanying intestinal obstruction is much discussed. This feature is not peculiar to intestinal obstruction. It follows injection of histamine in animals (Drake and Tisdall,<sup>14</sup> Hashimoto<sup>15</sup>) and is a prominent feature in shock resulting from insufficiency of the adrenal cortex (Banting and Cairns<sup>16</sup>). The blood chlorides are decreased in persons with many severe illnesses, including venous stasis, diabetic intoxication, pneumonia, pleurisy, burns, mercuric poisoning, eclampsia and other toxemias of pregnancy, anaphylactic shock, serum disease, etc (Peters and Van Slyke<sup>17</sup>). It is of interest to note that these conditions frequently produce shock, with hemoconcentration and characteristic postmortem appearances (Atchley,<sup>18</sup> Eppinger,<sup>19</sup> Moon<sup>20</sup>). A decrease in blood chlorides is not a distinctive feature of intestinal obstruction but is a feature in common with other conditions terminating in circulatory disturbances of the shock type. The same statement applies with equal force to the high non-protein nitrogen content of the blood. It also is found regularly in shock from diverse causes.

#### POSTMORTEM OBSERVATIONS ON ANIMALS WITH INTESTINAL OBSTRUCTION

Experimental obstructions were made in dogs to provide material for observations on the associated pathologic changes. With the animal under ether anesthesia and with aseptic technic, a tape was tied about a loop of bowel immediately below the mesenteric root. The included length of bowel ranged from 8 to 36 inches.

14 Drake, T. G. H., and Tisdall, F. F. *J. Biol. Chem.* **67** 91, 1926.

15 Hashimoto, H. *J. Pharmacol. & Exper. Therap.* **25** 381, 1925.

16 Banting, F. G., and Cairns, S. *Am. J. Physiol.* **77** 100, 1926.

17 Peters, J. P., and Van Slyke, D. D. *Quantitative Clinical Chemistry*, Baltimore, Williams & Wilkins Company, 1931.

18 Atchley, D. W. *Medical Shock*, *J. A. M. A.* **95** 385 (Aug. 9) 1930.

19 Eppinger, Hans. *Wien klin. Wchnschr.* **47** 10 and 355, 1919.

20 Moon, V. H. *Das Schocksyndrom*, *Deutsche med. Wchnschr.* **60** 1667 (Nov. 2) 1934.

as computed by Cannel, Hartman and du Nouy, (b) du Nouy's ideal algebraic equations for the rate of healing or cicatrization of sterile wounds must be corrected for a constant error when physical rather than chemical agents (antiseptics) are employed

New geometric curves are derived which it is claimed express more accurately the ideal rate of wound healing than those formerly given by Cannel and Hartman

The several actions through which elastic adhesive plaster exerts a favorable influence on wound healing are critically analyzed

**Histologic Examination** In the lung there was moderate congestion of the capillaries and venules and moderate edema of the alveoli and bronchial mucosa. There were scattered capillary hemorrhages. The mucosa of the unobstructed bowel showed marked congestion, slight edema and capillary hemorrhages. The venules and capillaries of the papillae were markedly distended and tortuous (fig 3). There was moderate congestion of the mucosa of the stomach. The pulp of the spleen was anemic. In the kidney there were marked congestion, edema, capillary hemorrhages and marked parenchymatous degeneration. The liver showed moderate congestion of the sinusoids. The heart muscle, adrenal glands and pancreas showed no changes.

**Dog 171**—This was a mongrel weighing 21 pounds (9.5 Kg). The red cell count was 8,000,000, the pulse rate 80, the respiratory rate 40 and the temperature 103 F.

On February 6, at 8 00 a m., about 3 feet (90 cm.) of the upper part of the small bowel was included in a loop ligated with tape. At 1 30 p m. examination revealed that the red cell count was 9,600,000, the pulse rate 108, the respiratory



Fig 2—Photograph showing congestion and hemorrhage of the mucosa of the unobstructed portion of the bowel of dog 170 compared with the small bowel from a normal dog (below)

rate 48 and the temperature 103.5 F. The dog was inactive and listless and vomited frequently. At 2 30 p m., 10 cc of a 1 per cent neutral solution of trypan blue was given intravenously. At 7 30 p m., the dog was comatose and moribund. The red cell count was 9,980,000, the pulse rate, 120, the respiratory rate 40 and the temperature 102.5 F.

**Postmortem Examination**—There was no fluid in the pleural cavities. The pleural surfaces of the lungs contained petechial hemorrhages. There was moderate congestion of the lung substance. There were petechial hemorrhages and marked bluing of the endocardial surfaces. The obstructed loop of bowel was greatly distended and intensely hemorrhagic. The peritoneal cavity contained about 150 cc of thin blood-tinged fluid. There was no peritonitis. The entire gastro-intestinal mucosa above and below the obstructed loop was intensely colored with the trypan blue. It contained numerous ecchymoses and was swollen and edematous. The liver and kidneys were congested and mottled with hemorrhagic areas. The kidneys and bladder showed marked staining with the trypan blue.

In articles dealing with intestinal obstruction a few of the authors have commented on the shocklike manifestations, but the majority of the reports have contained no suggestion that the shock syndrome has been recognized. There is general agreement that in dogs with intestinal obstruction at a high level there are vomiting, tremors and weakness the pulse becomes rapid and weak, and the blood pressure falls. The blood becomes concentrated its nonprotein nitrogen content increases and the chloride content decreases. The urine is scanty and may contain albumin or blood. Coma or lethargy precedes death. There is agreement that the same features follow the intravenous injection of various preparations of intestinal contents from a closed or strangulated loop. Stone and his associates<sup>2</sup> attributed this to alteration of digestive secretions and perhaps to absorption of products of protein cleavage from the closed loop. Gerard<sup>3</sup> attributed the intoxication to the liberation of histamine and other products of protein cleavage from the wall of the obstructed bowel. He showed that both histamine and substances from obstructed bowels produce a fall in blood pressure and temperature, rapid respiration, vomiting, bloody diarrhea decreased coagulation of the blood and hemoconcentration. Marked engorgement of the gastro-intestinal mucosa was recorded as a postmortem feature following such injections. Some workers produced these manifestations by intravenous injections of bacteria or their products. Numerous experiments of these types are on record. Apparently none of the authors were aware that each of these procedures will produce shock and that the manifestations described are characteristic of the shock syndrome. Detailed descriptions of the postmortem observations, with particular reference to visceral circulatory changes, would be most enlightening in such experiments. Unfortunately, these were not included in the published data.

#### CHANGES CHARACTERISTIC OF SHOCK

Most of the studies on intestinal obstruction were published before it was recognized that shock is accompanied by characteristic changes demonstrable by postmortem examination. It seems remarkable that these changes have so long escaped the attention of those interested in such conditions. Heubner (1907)<sup>4</sup> produced fatal shock by intravenous injection of gold chloride and gave the earliest description we have found of the visible changes characteristic of shock. The finest venules especially in the abdominal viscera, were heavily congested

<sup>2</sup> Stone, H. B., Bernheim, B. M., and Whipple, G. H. *Bull. Johns Hopkins Hosp.* **23** 159, 1912. *Ann. Surg.* **59** 715, 1914.

<sup>3</sup> Gerard, R. W. *Lethal Agent in Acute Intestinal Obstruction*, *J. A. M. A.* **79** 1581 (Nov. 4) 1922.

<sup>4</sup> Heubner, W. *Arch. f. exper. Path. u. Pharmacol.* **56** 370, 1907.



*Postmortem Examination*—The visceral and parietal pleurae were greatly congested and were stained with trypan blue. About 100 cc of blood-tinged bluish fluid was in each pleural cavity. There were petechial hemorrhages in the pleura and in the lung substance. The pericardium was congested, contained petechial hemorrhages and was moderately stained with blue. There was intense blue staining of the parietal wall and of the visceral peritoneum. There were marked congestion and bluing of the mucosa of the stomach. The obstructed portion of the bowel was intensely hemorrhagic and distended. The internal and external surfaces of the unobstructed bowel were greatly congested, edematous and intensely stained with blue. The peritoneal cavity contained about 150 cc of blood-tinged fluid. There was no peritonitis. The liver and kidneys were markedly congested. The kidneys were stained markedly with blue. The lining of the bladder was moderately congested and stained with blue.

*Microscopic Examination* In the lung there were diffuse congestion, scattered capillary hemorrhages and slight edema. The pulp of the spleen was anemic. In the small bowel there were marked congestion, edema and capillary hemorrhages of the mucosa. There was moderate congestion of the mucosa of the stomach. The kidney showed marked congestion and parenchymatous degeneration. There was slight congestion of the liver. In the bladder there was marked congestion of the venules and capillaries of the lining. The heart muscle, skeletal muscle and adrenal glands showed no visible change.

*Experiments on Other Dogs*—Six other dogs, 174 to 179 inclusive, were treated in exactly the same fashion and with exactly similar results, except that in a few instances trypan blue was not given. The evidences of illness and the gross and microscopic changes were not different in any particular from those reported in the protocols of the previous experiments. The time elapsing between the operation and death ranged from sixteen to thirty hours. These dogs did not die of peritonitis. They showed the same characteristics as are seen in the shock syndrome produced by various means.

In another experiment injections of aqueous extracts of intestinal mucosa were tested for their effects on blood pressure. The fresh duodenum and jejunum from a normal dog were opened and washed free from their contents. The mucosa was scraped with a dull knife, and one volume of the scrapings was suspended and vigorously shaken with four volumes of physiologic solution of sodium chloride. This was centrifugated at high speed for ten minutes, and the clear supernatant fluid was injected intravenously into dogs which had been anesthetized with ether and had a cannula in the carotid artery recording blood pressure through a mercury manometer. An aqueous extract of mucosa from an obstructed loop of bowel was prepared and used in exactly the same manner. The mucosa from such obstructed loops is diffusely hemorrhagic and partially necrotic and contains many bacteria. Hence, as may be expected, its effects are more severe.

Dog 180 was given 10 cc of extract of normal mucosa. The blood pressure promptly fell 56 mm and then gradually returned to normal. In dog 181 and 182 the blood pressure fell 70 mm and 62 mm, respectively, following the injection of the same volume of extract. In each instance the blood pressure returned to normal within thirty minutes. At subsequent postmortem examinations there was slight diffuse congestion of the lungs, gastro-intestinal mucosa and liver. No other significant changes were present.

Dog 183 received 10 cc of extract of mucosa from an obstructed loop. This produced a rapid fall in blood pressure ending in death almost immediately. Dog

regularly by the pathologists. None of these observers commented on the significance of these visible evidences or emphasized their etiologic relationship to the mechanism by which shock results. Moon and Kennedy<sup>12</sup> produced shock by various methods in dogs and found regularly the same changes as described by Heubner. Recently one of us (Dr. Moon<sup>13</sup>) summarized as follows the changes accompanying the shock syndrome variously produced:

The veins in subcutaneous and peripheral areas are collapsed and relatively bloodless. The viscera are deeply congested and have a purplish, diffuse, cyanotic color. This is especially prominent in the lungs, liver and gastro-intestinal tract. The venules of the visceral peritoneum are engorged and distended. Those along the mesenteric attachment are especially prominent. Usually the spleen is contracted and bloodless, though occasionally it also is engorged. There are varying quantities of thin blood-tinged fluid in the peritoneal, pleural and sometimes in the pericardial cavities. The mucosae of the respiratory and gastro-intestinal tracts are swollen and have the appearance of red velvet. There are numerous petechial hemorrhages in the lungs, in the pleural and pericardial surfaces, in the intestinal mucosa, occasionally in the lining of the gall and urinary bladders and in the meninges. Edema of the lungs and mucosae and serous effusions are most marked when shock develops gradually and death is not immediate. When shock ending in death develops rapidly congestion and capillary hemorrhages are marked and edema is a less prominent feature. The fluid present in the stomach usually contains "coffee-ground" flocculi which give a positive test for hemoglobin. The fluid in the stomach and bowel contains quantities of serum albumin. The undiluted fluid often forms a solid coagulum when heated.

On microscopic examination there are marked dilatation and engorgement of the capillaries and venules in each of the organs mentioned. There are numerous minute areas of hemorrhage, apparently from dissolution of capillary walls, and tissue edema is present in varying degrees. The adrenals participate in these circulatory changes in a degree similar to that seen in other organs, but they show no other changes.

These observations indicate a widespread loss of tonus affecting the capillaries and venules. The circulatory disparity in this instance results from an increased volume-capacity of the vascular system or, what is equivalent, from inability of the vascular system to contract with its normal tonus on the contained blood.

There was evidence that the minute vessels were abnormally permeable to blood plasma. This gave rise to edema, serous effusions, and to the transudation of fluid from the blood into the gastro-intestinal canal. Such loss of fluid lowers the blood volume and produces hemoconcentration.

The fact that the spleen usually does not share in the visceral congestion is significant. The spleen acts as a reservoir for blood not needed by the system. Shock is similar to hemorrhage in its effects, and the spleen discharges its reserve of blood in a physiologic effort to meet

<sup>12</sup> Moon, V. H., and Kennedy, P. J. Pathology of Shock, *Arch. Path.* **14** 360 (Sept.) 1932.

<sup>13</sup> Moon, V. H. Shock Syndrome in Medicine and Surgery, *Ann. Int. Med.* **8**:1633 (June) 1935.

these necropsies were made before it was recognized that visible circulatory changes regularly accompany the shock syndrome. Such changes as marked visceral congestion, edema of mucosae and of the lungs, capillary hemorrhages in mucous and serous surfaces and blood-tinged serous effusions were noted frequently in these postmortem records, though without comment on their significance. The following case is illustrative.

A man, aged 54, became weak and sick while working. He had abdominal pain and an urgent desire to defecate. Nausea and vomiting developed, and there was frequent passage of watery feces. The abdomen was somewhat distended and tender, but there was no rigidity. Tympany and active peristalsis were noted. On the following day, the bowel movements had ceased, but the other symptoms increased in severity. The skin was cold and clammy, the nail beds and lips became cyanotic and the temperature was subnormal. The blood pressure was 116 systolic and 88 diastolic, and the radial pulse rate was 114. The red cell count was not recorded. The vomitus was voluminous and contained visible blood. A stomach tube was introduced, and large quantities of fluid were removed from the stomach. Moderate congestion and edema of the lungs were noted. Intravenous injections of dextrose in saline solution and stimulants were given without benefit. On the next morning, the blood pressure was not measurable. The radial pulse was very rapid and barely palpable. The patient became comatose and died about sixty-five hours after the onset of illness. The chief of staff noted on the record: "This man was in a state of shock."

At necropsy a loop of ileum about 7 feet (213 cm) long was found obstructed by adhesions. The mucosa of this was markedly hemorrhagic and contained areas of necrosis. Thrombi were present in the small mesenteric vessels. The fluid from the stomach contained "coffee-ground" flocculi. The mucosa of the stomach and that of the unobstructed bowel were swollen, deeply congested and ecchymotic. The peritoneal cavity contained blood-tinged fluid, but there was no evidence of generalized peritonitis. The lungs were markedly congested, had increased in weight and contained numerous small hemorrhagic areas. Moderate pulmonary edema was present. The liver and kidneys were congested. The spleen was not congested but was tough and flabby in consistency. The adrenal glands showed no visible changes.

Details of other cases of this type would be a repetition of observations well established and recognized by surgeons. The changes observed post mortem do not differ from those usually described. They are those which regularly accompany the shock syndrome, whether it occurs clinically or as a result of experimentation.

#### COMMENT

The shock syndrome is a grave circulatory disturbance, which may originate in different ways. It arises whenever there is a serious disparity between the volume of blood and the volume capacity of the vascular system. Such a disparity may develop from a decreased volume of blood, from an increased volume capacity of the vascular system or

(20 to 90 cm) in different dogs, and the tape was sufficiently tight to obstruct the lumen. No kymographic records were made since it was desired to avoid the complicating effects of prolonged anesthesia, which often produces dilatation and engorgement of minute vessels, resulting in shocklike phenomena. Such effects are usually present if deep narcosis with one of the barbiturates has been employed. Red cell counts and estimations of hemoglobin were made before and at intervals following the operations. Hemoconcentration served in these as in previous experiments to indicate the development of circulatory failure. A few representative protocols of these experiments follow.

**Dog 170**—This was a mongrel hound weighing 25 pounds (11.3 Kg). The red cell count was 6,800,000, the pulse rate 100, the respiratory rate 56 and the temperature 101.4 F.

On February 5, at 8:00 a. m., with the animal under ether anesthesia a loop at the upper end of the jejunum 8 inches (20 cm) in length was ligated with tape. The dog had marked tremors, was listless and inactive and vomited occasionally.



Fig 1—Photograph showing congestion of the lungs of dog 170 compared with those of a normal dog (left).

At 4:30 p. m. the red cell count was 8,890,000, the pulse rate 170, the respiratory rate 40 and the temperature 101.8 F. On February 6, at 8:00 a. m., the dog was found in his cage dead and cold.

**Postmortem Examination**—The lungs, pleura and pericardium were intensely congested (fig 1). There was no free fluid in the chest cavities. There was 125 cc of blood-tinged fluid in the peritoneal cavity. The peritoneum was markedly congested throughout but showed no evidence of peritonitis. The venules along the mesenteric attachment were distended and engorged. The ligated loop of bowel was distended, intensely hemorrhagic and very dark. The peritoneum covering the entire bowel tract was reddish purple. The mucosa of the bowel, both above and below the obstruction, was intensely congested and diffusely hemorrhagic (fig 2). The mucosa of the stomach was greatly congested and purple. There was marked congestion of the liver and kidneys. The spleen was dry, contracted and bloodless. The adrenal glands appeared normal.

normal capillary walls but will permeate the tissue spaces where permeability of the capillaries is increased. In our experiments there was marked staining of the serous and mucous surfaces, kidneys, bladder and other tissue in animals brought to death by intestinal obstruction. This observation supplied visible evidence of increased permeability of the capillaries in extensive areas.

The hemoconcentration accompanying intestinal obstruction has been assigned to loss of fluid by vomiting. Such fluid comes from the blood, largely because of permeability of the capillaries. The fluid found in the stomach and frequently that in the bowel contain quantities of albumin. The "coffee-ground" vomitus from such patients contains hemoglobin and serum albumin which have escaped through the walls of the capillaries. Such loss of fluid is an important factor contributing to decreased blood volume and to hemoconcentration. The effusions into serous cavities and the edema of the lungs and mucosae are likewise important factors. The combined effect of loss of blood volume by transudation and of increased volume capacity due to atony of capillaries and venules produces a circulatory insufficiency which manifests itself in the shock syndrome.

#### CONCLUSIONS

There is much evidence that death following intestinal obstruction results from circulatory failure of the shock type.

The physiologic disturbances following intestinal obstruction are those usually seen in the shock syndrome.

The gross and microscopic visceral changes are identical with those which accompany shock produced by various means. These changes are marked distention and engorgement of the capillaries and venules in the viscera, edema and ecchymoses of the lungs and gastro-intestinal mucosae and effusions into serous cavities. Evidence of injury to the capillaries is seen in the capillary hemorrhages, the formation of edema fluid of high protein content and the rapidity with which colloidal dyes escape from the blood into the tissues.

The probable cause of the shock syndrome following intestinal obstruction is intoxication by histamine, by other products of injured tissue and by bacteria and their products absorbed from the obstructed bowel. Any of these agents alone will produce the shock syndrome in animals. Debate concerning the relative clinical importance of these agents is not profitable.

Intestinal obstruction is one of the many conditions which will produce characteristically the shock syndrome.

There was also staining of the mesentery and of the retroperitoneal lymph nodes. The adrenal glands were slightly congested but otherwise appeared normal.

**Histologic Examination** In the lung there were intense congestion of the venules and capillaries, numerous capillary hemorrhages and beginning edema. The mucosa of the unobstructed bowel was intensely congested and contained numerous capillary hemorrhages. The stomach showed marked congestion and capillary hemorrhages in the mucosa. In the kidney there were marked congestion, numerous capillary hemorrhages and marked parenchymatous degeneration. In the liver there were congestion of sinusoids and parenchymatous degeneration. The heart muscle, pancreas and adrenal glands were normal.

**Dog 173**—This was a male mongrel weighing 22 pounds (10 Kg). The red cell count was 6,350,000, the pulse rate 64, the respiratory rate 29 and the temperature 103.2 F.

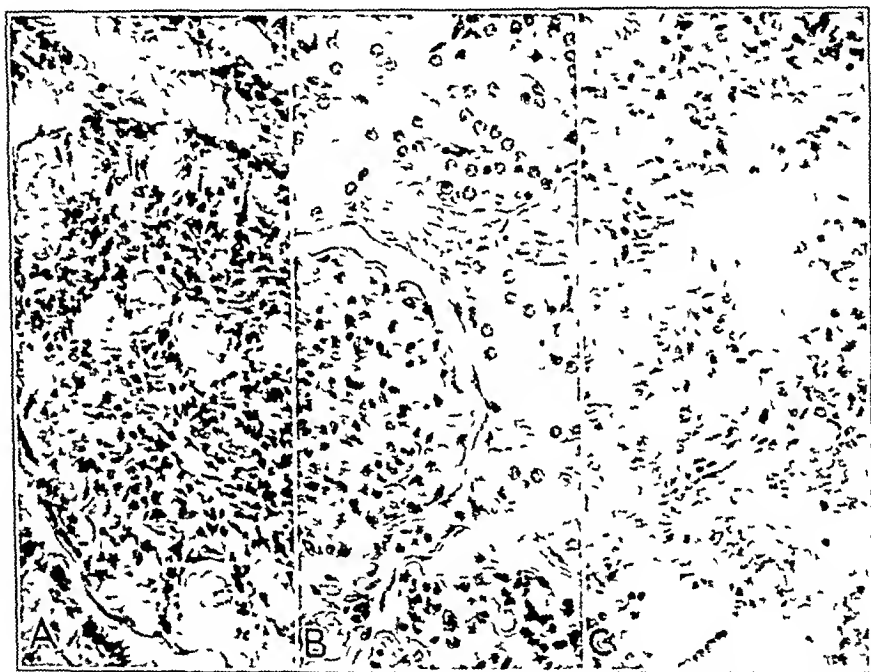


Fig 3—Photomicrographs of mucosa of the unobstructed bowel (A), the kidney (B) and the lung (C) from a dog with intestinal obstruction at a high level. Note the edema and the marked distention of the papillary venules of the mucosa. The glomerular and intertubular capillaries are congested, and there are congestion and capillary hemorrhages in the lung.

On February 13, at 4:00 p.m., a loop of the intestine approximately 10 inches (25 cm) in length was ligated with tape. The duration of the operation was ten minutes. On February 14, at 8:00 a.m., the red cell count was 8,880,000, the pulse rate 85, the respiratory rate 25 and the temperature 103 F. The dog showed the usual evidences of illness, including muscular tremors, frequent vomiting, rapid pulse, weakness and apathy. At 5:00 p.m., the red cell count was 10,000,000, the pulse rate 90, the respiratory rate 30 and the temperature 102.7 F. Ten cubic centimeters of a 1 per cent neutral solution of trypan blue was injected intravenously. At 9:00 p.m., the dog was semicomatose and apparently moribund. The red cell count was 10,900,000, the pulse rate 140, the respiratory rate 18 and the temperature 103.8 F.

TABLE 1—Observations on 17 Personally

	Date of Admission	Age and Sex	Previous Operations	Symptoms on Admission	Duration of Symptoms	Physical Findings	Preoperative Diagnosis	Laboratory Data
1	7/14/31	23 M	Appendectomy 4 yr before, followed by fecal fistula, three attempts to close fistula unsuccessful	Fecal discharge from abdominal wound loss of 40 lb (wt 80 lb), abdominal cramps, general weakness T, 99 F P R, 80 R R, 20	4½ yr	Debilitated 3 scars in lower right quadrant with fecal fistula at lower end of r. McBurney scar entire abdomen very tender lungs normal	Fecal fistula of tuberculous nature	Hem 77% R B C 4,250,000 W B C 10,600 poly 77% mono 7% lymph 16% urine and feces normal
2	7/ 5/32	26 M	None	Pains in right lower quadrant with nausea and vomiting, no previous attack T 100 F P R 90 R R 22	3 da	Well developed acutely ill tenderness rigidity with rebound tenderness in right lower quadrant with slight distention	Acute appendicitis	Hem 92% R B C 4,800,000 W B C 18,200, poly 92% lymph 8% urine normal
3	9/ 4/32	16 F	None	Pains in right lower quadrant with nausea and vomiting 2 previous attacks T 99 F P R 100 R R 22	3 da	Weight 90 lb tenderness, rigidity with rebound tenderness in right lower quadrant with mass palpable moderate distention	Acute appendicitis	Hem 75% R B C 3,900,000 W B C 6,700 poly 60% lymph 29% mono 11% urine normal
4	9/13/32	24 F	None	Pains in right lower quadrant vomiting no previous attack T 100 F P R 112 R R 24	4 da	Well developed tenderness, rigidity with rebound tenderness in right lower quadrant with moderate distention	Acute appendicitis	Hem 80% R B C 3,953,000 W B C 20,100 poly 94% lymph 3% mono 3% urine normal
5	11/13/32	34 M	None	Pains in right lower quadrant with nausea and vomiting no previous attack T 102 F P R 108 R R 22	2 da	Well developed tenderness, rigidity with rebound tenderness in right lower quadrant, no distention	Acute appendicitis	Hem 100% R B C 5,000,000 W B C 16,200 poly 90% lymph 10% urine normal
6	11/15/32	14 F	None	Pains in right lower quadrant with nausea and vomiting no previous attack T 100 F P R 110 R R 22	6 da	Well developed tenderness rigidity of entire lower quadrant with marked rebound tenderness slight distention	Acute appendicitis	Hem 99% R B C 4,990,000 W B C 11,900, poly 87% lymph 10% mono 3% urine normal
7	7/30/33	38 M	None	Pains in right lower quadrant and epigastrium for past year with nausea and vomiting at times T 99 F P R 70 R R 20	1 yr	Well developed marked tenderness in right lower quadrant with hyperesthesia roentgen examination showed pathologic changes in appendix	Chronic appendicitis	Hem 100% R B C 4,950,000 W B C 11,200 poly 68% lymph 28% mono 4% urine normal
8	11/ 2/33	35 M	None	Intermittent pains about umbilicus with nausea and constipation loss of 10 lb in 6 mo T 99 F P R 84 R R 24	3 yr	Well developed tender and distended abdomen with visible peristalsis no definite mass palpable, enema resulted in no return and increased pains	Partial intestinal obstruction	Hem 100% R B C 5,150,000 W B C 13,600 poly 67% lymph 0% mono 3% urine normal

184 received the same dose, with a similar result. Dog 185 was given 5 cc of the same extract. This produced an immediate fall in blood pressure ending in death in ten minutes. At postmortem examination there was marked diffuse congestion of the lungs, bronchial mucosa, intestinal mucosa, liver and kidneys. The venules along the mesenteric attachment were engorged and prominent. The adrenal glands were slightly congested. The spleens were contracted and bloodless. Microscopically there were marked congestion and numerous capillary hemorrhages in the lungs and gastro-intestinal mucosae. No edema was present.

This experiment illustrates the fact that extracts of normal tissues, in this instance intestinal mucosa, produce a fall in blood pressure. Whether this is due to histamine or to products of protein cleavage produced by autolysis is not apparent. Probably it is due to the combined effects of both. The extract of mucosa from the obstructed bowel would probably not contain more histamine than normal mucosa, but it would contain more products of necrotic disintegrating tissue. The observation is not new that extracts of disintegrating necrotic tissues are toxic and will produce a fall in blood pressure and other manifestations of shock if introduced into the circulation. In our experiment the extract of obstructed mucosa was much more potent than that of normal mucosa under like conditions.

It is probable that the absorption of substances from strangulated loops takes place in part via the blood and lymph channels if these are not obstructed and in part by diffusion into the peritoneal cavity with absorption through the peritoneal surfaces. The products of bacterial growth will be factors of importance in proportion to their amount and toxicity. The combined effects of histamine, products of disintegration of tissue and products of bacterial activity, any one of which alone will produce shock, will account for the clinical manifestations and postmortem observations in cases of intestinal obstruction or strangulation, whether occurring spontaneously or experimentally.

It has been noted repeatedly that the effects of simple obstruction are much less marked than those of strangulation. Apparently the mechanism is similar, and the difference is quantitative rather than qualitative.

#### INTESTINAL OBSTRUCTION IN HUMAN BEINGS

In a survey of the records of postmortem examinations of the past ten years in Jefferson Hospital, twenty-six cases were found in which intestinal obstruction was a chief or a contributory cause of death. The obstructions were of various degrees, types and locations, and the duration of illness varied. Peritonitis was a complicating factor in many cases. The cases in which obstruction was a major factor had the usual clinical characteristics. Such features as terminal circulatory failure, with rapid weak pulse, falling blood pressure and pulmonary congestion and edema, were prominent in the clinical histories. The majority of



TABLE 1—Observations on 17 Personally

	Date of Admission	Age and Sex	Previous Operations	Symptoms on Admission	Duration of Symptoms	Physical Findings	Preoperative Diagnosis	Laboratory Data
9	12/18/33	7 M	None	Pains in right lower quadrant with nausea and vomiting 1 previous attack T 103.6 F P R 130, R R 24	2 da	Well developed tenderness, rigidity with rebound tenderness in right lower quadrant	Acute appendicitis	Hem 102% R B C 5,100,000 W B C 20,800, poly 89% lymph 4% mono 7% urine normal
10	1/18/32 (1st adm)	37 F	None	Pains in right lower quadrant with nausea and vomiting constipation several previous attacks in past year T 98.6 F P R 120 R R 28	2 wk	Well developed tenderness and rigidity with rebound tenderness in right lower quadrant moderate distention	Acute appendicitis	Hem 93% R B C 4,200,000 W B C 15,800 poly 85% lymph 12% mono 3% urine normal
	2/12/34 (2d adm)		Ileocolostomy 25 days before	Diffuse abdominal cramps and vomiting T 99.8 F, P R 100, R R 24		Marked tenderness in right lower quadrant, moderate distention		W B C 18,200, poly 87% lymph 13%
11	5/10/34	21 F	None	Pains in right lower quadrant with nausea and vomiting 3 attacks in past 4 yr T 100.8 F P R 80, R R 20	4 da	Well developed tenderness, rigidity with rebound tenderness in right lower quadrant slight distention	Acute appendicitis	Hem 98% R B C 4,650,000 W B C 12,800 poly 71% lymph 21% mono 8% urine normal
12	7/27/34	23 M	None	Pains in right lower quadrant with vomiting 1 attack 6 mo before T 99.8 F P R 90 R R 20	3 da	Well developed tenderness and rigidity with rebound tenderness in right lower quadrant	Acute appendicitis	Hem 118% R B C 5,210,000 W B C 20,000 poly 80% lymph 20% urine normal
13	7/29/34	39 F	None	Pains in right lower quadrant with vomiting no previous attacks T 101 F P R 96, R R 24	3 da	Well developed and obese tenderness and rigidity with rebound tenderness in right lower quadrant	Acute appendicitis	Hem 96% R B C 4,800,000 W B C 16,000 poly 88% lymph 12% urine normal
14	9/20/34	49 M	Appendectomy in 1910	Irregular sharp pains in right lower quadrant worse in past 6 mo loss of 15 lb in 2 wk constipation & rigidity of gastro intestinal tract normal T 99.2 F P R 86 R R 20	2 yr	Well developed old McBurney scar, irregular, slightly mobile very tender doughy mass in right lower quadrant which was dull on percussion moderate distention of abdomen	Nonspecific regional ileitis or carcinoma of cecum	Hem 96% R B C 4,800,000 W B C 7,100 poly 69% lymph 24% mono 7% urine normal
15	10/12/34	28 M	Appendectomy 8 mo before followed by fecal fistula	Fecal discharge from abdominal wound cramps, vomiting obstipation for 3 da in spite of enema T 102 F P R 100 R R 28	3 da	Well developed poorly healed scar of right rectus muscle with fecal fistula in center tenderness and rigidity in right lower quadrant moderate distention with visible peristaltic waves	Acute intestinal obstruction and fecal fistula	Hem 100% R B C 5,000,000 W B C 19,800 poly 89% lymph 6% mono 5% urine normal
16	11/ 6/34	26 M	None	Recurrent pains in right lower quadrant for past 4 mo relieved by diarrhea and nausea T 101 F P R 110 R R 28	2 da	Well developed tenderness rigidity with rebound tenderness in right lower quadrant	Acute appendicitis	Hem 88% R B C 4,800,000 W B C 16,300 poly 86% lymph 14% urine normal
17	1/ 7/35	30 M	None	Pains in right lower quadrant nausea and vomiting no previous attack T 99.8 F P R 88, R R 24	3 da	Well developed tenderness rigidity with rebound tenderness in right lower quadrant, slight distention	Acute appendicitis	Hem 100% R B C 5,000,000 W B C 7,200 poly 72% lymph 21% mono 7% urine normal

from combinations of these. In human patients with shock and in animals with experimentally induced shock there is visible postmortem evidence of an increased volume capacity of the vascular system. This is seen in the abnormal dilatation of the venules and capillaries. A decreased volume of blood may result from loss of plasma by transudation through capillary walls. Evidence of this is seen in the edema of mucosae, in the effusions of serum into cavities lined with serous membrane and pulmonary alveoli and in the numerous capillary hemorrhages occurring in mucous and serous surfaces and in the parenchyma of organs.

When capillaries are injured, by whatever means, the permeability of their walls is increased (Landis<sup>21</sup>). Injury to the capillaries may result from a wide variety of agents. These include various chemical poisons, such as mercury bichloride, arsenical compounds, gold salts, alcohol and anesthetic drugs, such as barbital. Histamine, peptone, products of protein cleavage and extracts of various tissues cause injury to the capillaries, deficiency of oxygen of moderate degree and short duration will cause capillaries to dilate and then permeability to be increased (Krogh,<sup>22</sup> Landis<sup>21</sup> and others).

When permeability of the capillaries is increased in extensive areas, the transudation of plasma through their walls causes edema in the tissues and increases the concentration of the blood. The dilated capillaries and venules are filled with viscid concentrated blood, and the heart is unable to maintain normal blood pressure because of insufficient return of blood from the periphery. The heart is not a suction pump, it cannot draw blood out of the tissues but can only pump the blood which is returned to it. As the circulation becomes ineffective, lack of oxygen contributes to further capillary atony, and the circulatory disturbance becomes more grave (Cannon<sup>10</sup>).

If lowered blood volume and hemoconcentration are produced by plasmapheresis without injury to the capillaries the animal may return to normal spontaneously or following the therapeutic administration of fluid. Fluid is absorbed if given by mouth or by hypodermoclysis, and fluids injected intravenously are retained in the circulation. In shock fluids are neither absorbed nor retained. Injection of them into the blood merely increases the edema. It appears that an essential factor by which shock develops and progresses is increased permeability of the capillaries.

Many workers have used colloidal dyes as indicators of permeability of the capillaries. Such dyes as trypan blue do not pass readily through

<sup>21</sup> Landis, E. M. *Physiol. Rev.* **14** 404, 1934.

<sup>22</sup> Krogh, A. *The Anatomy and Physiology of Capillaries*, ed. 2, New Haven, Yale University Press, 1929.

Our cases occurred mainly in young patients, 11 in males and 6 in females. The duration of symptoms varied from a few days to four years before operation was performed.

TABLE 2—*A Summary of the Personally Observed Cases*

	Number of Cases
Age incidence	
1 to 10 years	1
11 to 20 years	2
21 to 30 years	8
31 to 40 years	5
49 years	1
Sex	
Males	11
Females	6
Duration of symptoms	
7 days or less	6
4 to 6 months	5
6 to 12 months	3
2, 3 and $4\frac{1}{2}$ years	3
Abdominal pain	
Generalized	1*
Localized in right lower quadrant	14
Diarrhea	1
Nausea	11
Vomiting (2 without nausea)	13
Previous attacks of abdominal cramps (prior to acute attacks that caused hospitalization)	10
Loss of weight (all advanced stage)	3
Previous operation (appendectomy complicated by fecal fistula 8 months before, 4 years before, 24 years before)	3
Tenderness	17
Spasticity (right lower part of abdomen)	13
Rebound tenderness	13
Distention	10
Mass (palpable on both abdominal and rectal examination)	2
Visible peristalsis	2
Fecal fistulas	2
Temperature	
Below 99 F	1
99 to 100 F	13
100 F or above	2
Pulse rate	
80 or less	3
80 to 100	8
100 to 120	6
Respiratory rate (no elevation in any case)	
White blood cell count and differential	
8 000 or less	2
8 000 to 10 000	1
10 000 to 12 000	2
12 000 to 14 000	2
14 000 to 16 000	2
16 000 to 18 000	3
18 000 to 20 000	3
20 000	2
Procedures performed	
Simple appendectomy	7
One stage resection (including 2 cases of fecal fistula)	7
Two stage resection	3

The outstanding symptoms were pain in the right lower abdominal quadrant, nausea and vomiting. Physical examination revealed abdominal tenderness in all the cases, spasticity and rebound tenderness in 13 and distention in 10. Visible peristalsis was noted in 2 cases, a mass palpable on abdominal and rectal examination was encountered

# REGIONAL ILEITIS

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In the past few years a number of papers dealing with the question of nonspecific inflammatory lesions in the gastro-intestinal tract have appeared. Some of the papers dealt with the subject at length. Others reported only a few cases with comments. A great deal remains to be clarified, especially regarding the early phases of the disease. More specific information is needed relating to (1) prognosis as to life, (2) incidence of recurrence even after radical surgical intervention, and (3) the end-results in cases of the early stages noted at operation, in which no resection or other intestinal procedure is done. Criteria for clinical diagnosis must be established as it becomes more obvious daily that the condition is not uncommon and must surely be noted from time to time in the routine experience of the general practitioner. He must be prepared to recognize the syndrome or at least the possibilities thereof. He should know what diagnostic steps to take in an attempt to answer the foregoing questions as intelligently as is possible. With these needs in mind we have reviewed the publications on intestinal granuloma, studied the reports of cases and tabulated the clinical facts derived therefrom. To this survey we have added observations on 17 cases of our own, which we shall discuss in greater detail.

From July 14, 1931 to Dec 6, 1934, we encountered 17 instances of a peculiar inflammatory lesion localized in the terminal portion of the ileum ranging in severity from the mildest type of inflammatory process to the severest type of deformation of the wall and lumen of the intestine, with ulceration and in some cases, fistulas following perforation. These cases we believe can properly be considered under the heading of nonspecific inflammatory disease of the intestinal tract, previously described by many authors. Although the lesion was recognized many years ago it is only within the last few years that interest in it has been stimulated by the appearance of reports of the lesion in the small intestine.

A synopsis of the histories of the 17 cases is given in table 1. In table 2, an analysis of these cases is presented.

mesenteric border, where the mesentery joins the serosa of the intestinal wall. The serosa is a mottled red. The mesentery is markedly thickened, and its glands are hyperplastic. The microscopic appearance of the early lesion as determined by biopsy (fig 1), is that of subacute nonspecific inflammation with beginning muscular hypertrophy. From a study of the various specimens encountered, the following deductions are made. The lesion is progressive. In the earliest stages it is present in the region of the ileocecal valve, from which there is exten-



Fig 1 (case 16) —Section of a biopsy specimen, showing subacute inflammation with fibrosis and hypertrophy of the musculature

sion orally. Usually oral to the main hypertrophic mass, small oval ulcerations ranging from 0.5 to 1 cm in diameter, are present on the mesenteric surface of the ileum. In the more advanced stages ulcerations are noted throughout the entire length of the hypertrophic mass. The normal intestinal folds disappear completely. Mucosal ulceration occurs. Because of the rounding off of the sharp edges of the remaining nonulcerated mucous membrane as it converges into the surrounding

*Observed Patients with Regional Ileitis*

Observations at Operation	Surgical Procedure	Pathologic Reports	Postoperative Course	Discharge	Present Status	Comment
Sigmoid flexure attached to cecum and terminal ileum, with multiple fistulous tracts and sinuses emptying into one large tract to opening in abdominal wall ileo colostomy to ascending colon	Sigmoid separated from cecum opening in sigmoid closed by purse string suture, entire ileocecal region excised, including fistulous tracts and mesentery 3 layered closure of open ends of intestine, cigaret drain to abdomen	Chronic ulcerating ileitis of nonspecific inflammatory origin tuberculous ileitis definitely ruled out	Drain removed on fifth day sutures removed on eighth day, uneventful recovery	8/31/31	11/30/34 wt 140 lb, bowel movement regular no complaint	Weight at discharge, 116 lb operation subsequently for ischioanal fistula with good result
Appendix injected large amount of serous fluid, about 1 ft from ileocecal junction, 3 ft of ileum involved in inflammatory thickening with edema of its mesentery and enlarged glands partial obstruction	Resection of involved ileum including its mesentery and glands, with an end to end ileo ileostomy smears for culture taken from abdomen, no drainage	Chronic nonspecific inflammation of ileum cultures of abdominal fluid negative	Sutures removed on eighth day uneventful recovery	7/19/32	12/3/34 no complaint bowel movement daily gain of 16 lb	Acute symptoms due to obstruction caused by the stenosing lesion
Enlarged mesenteric glands inflammatory mass of ileum, cecum and omentum with appendix normal but adherent to congested, thickened ileum, perforation of ileum near ileocecal junction walled off by omentum, with almost complete obstruction	Resection of terminal 9 in. of ileum and cecum, including enlarged glands, with side-to-side ileocolostomy to ascending colon, no drainage	Chronic nonspecific inflammation of ileum with superimposed subacute ulcerating lesions	Sutures removed on seventh day uneventful recovery	9/17/34	10/31/34 no complaint x rays showed well functioning stomach wt 122 lb	Weight at discharge, 102 lb, this case typifies ulcerating nature of lesion
Free serous fluid in abdomen appendix congested and adherent to mass consisting of ileum cecum, right tube and ovary, omentum terminal ileum enlarged inflamed and thickened	Resection of terminal 14 in. of ileum and cecum with end to side ileocolostomy to ascending colon cigaret drain inserted to abdomen	Chronic nonspecific inflammation of ileum with stenosis of ileocecal valve	Drain removed on fifth day sutures removed on seventh day uneventful recovery	9/26/32	10/31/34 bowel movement regular no complaint x rays showed good stomach gain of 10 lb	Acute symptoms due to obstruction at ileocecal valve
Free serous fluid, appendix congested terminal 12 in. of ileum inflamed slightly thickened, with edema of mesentery and enlarged glands no obstruction	Appendectomy insertion of cigaret drain into abdomen because of large amount of fluid one mesenteric gland removed for biopsy	No lesion of appendix acute nonspecific inflammation of lymph node	Drain removed on fifth day sutures removed on eighth day uneventful recovery	11/25/32	11/13/34 no complaint bowel movement regular, gain of 14 lb	Early stage of regional ileitis with acute symptoms
Large amount of sero hemorrhagic fluid injected appendix hemorrhagic markedly thickened, 14 in. of ileum, beginning 6 in. from ileocecal junction mesentery edematous, glands enlarged	Resection of involved ileum, including its mesentery and glands, with end to end ileo ileostomy, appendectomy, no drainage	No lesion of appendix chronic nonspecific ileitis, with superimposed acute purulent inflammation areas of necrosis and ulceration	Sutures removed on seventh day uneventful recovery	12/3/32	11/10/34 bowel movement regular no complaint gain of 24 lb	Ulcerating stage of regional ileitis provoking marked peritoneal reaction
Slight amount of serous fluid inflammation and slight thickening of about 4 in. of ileum about 1 ft from ileocecal junction moderate edema and enlarged glands in the vicinity of the involved ileum	Appendectomy excision of one mesenteric gland for biopsy, no drainage	Chronic appendicitis chronic nonspecific inflammation of lymph node	Sutures removed on seventh day uneventful recovery	8/12/33	12/10/33 no complaint bowel movement regular gain of 11 lb	Early stage of regional ileitis high voltage roentgen therapy to abdomen in 2 doses one week after leaving hospital
Moderate amount of serous fluid marked thickening inflammation of terminal 10 in. of ileum ileocecal glands enlarged and inflamed	Ileocolostomy of ileum 2½ ft from ileocecal valve to transverse colon no drainage (11/3/33)	Chronic nonspecific ileitis with trophic hyper trophy of the musculature	Sutures removed on seventh day, uneventful recovery	11/26/33	11/30/34 bowel movement regular no complaint gain of 18 lb	Two stage resection performed because of acute obstruction and patient's general condition
Second laparotomy flap bag same well functioning ileocolic stomach	Resection of terminal 15 in. of ileum, cecum and half of ascending colon, with closure of open ends, no drainage (11/14/33)		Sutures removed on eighth day uneventful recovery			

are seen in this section, whereas active peristalsis can be seen elsewhere. The mucosal ulcerations finally diminish in number, being replaced by an atrophic condition and a more marked stage of the polypoid hyperplasia previously described. Small tubercle-like structures develop on the serosal surface.

Perforation was seen in 2 cases in our series. In the first case the perforation was very extensive, involving several parts of the bowel.



Fig. 3 (case 15) —Low power magnification of the cross-section at (A) in figure 2, showing marked encroachment of the thickened wall on the lumen. The membrane is absent in places as a result of ulceration, at other points it seems polypoid.

at one time, the ileum, the cecum and the sigmoid flexure being involved. In the second case, only the ileum was involved. In both cases the perforation was of the chronic variety. We know of no case in which a free perforation in the peritoneal cavity was encountered in the acute

Observed Patients with Regional Ileitis—Continued

Observations at Operation	Surgical Procedure	Pathologic Reports	Postoperative Course	Discharge	Present Status	Comment
Appendix injected slight amount of serous fluid, terminal 5 in. of ileum inflamed slightly thickened, with enlarged inflamed glands at ileocecal angle	Appendectomy, excision of mesenteric gland for biopsy, no drainage	No lesion of appendix, acute nonspecific inflammation of lymph node	Sutures removed on seventh day, uneventful recovery	12/30/33	11/28/34 bowel movement regular, no complaint gain of 15 lb	Early stage of regional ileitis with acute symptoms 2 treatments with roentgen rays while in the hospital
Appendix injected and adherent serohemorrhagic fluid terminal 18 in. of ileum inflamed, thickened with obstruction at ileocecal valve enlarged mesenteric glands	Ileocolostomy of ileum 5 ft from ileocecal valve to transverse colon, no drainage (1/18/34)	Subacute non-specific ileitis with ulceration chronic obliterative appendicitis	Sutures removed on eighth day, collection evacuated from wound on tenth day	2/ 1/34	11/30/34 bowel movement regular, no complaint gain of 20 lb x rays showed good stroma	Two stage resection deemed advisable in the face of acute obstruction patient sent home after the first stage to get her in better shape for the second operation, but because of marked progression of the disease brought back sooner than planned
Mesenteric glands suppurating and walled off by omentum and small intestine, with necrosis and ulceration of involved ileum	Resection of terminal 18 in. of ileum, cecum and ascending colon, including suppurative glands, with closure of open ends, cigarette drain inserted (2/13/34)		Drain removed on eleventh day, wound healed slowly and drained for 4 wk	3/19/34		
Appendix injected moderate serous fluid, terminal 4 in. of ileum inflamed, thickened, with stenosis of ileocecal valve and marked enlargement of mesenteric glands	Resection of terminal 1 ft of ileum, cecum and portion of ascending colon, with ileocolostomy to transverse colon, no drainage	Subacute nonspecific ileitis, with ulceration and stenosis	Sutures removed on seventh day, uneventful recovery	5/27/34	10/30/34 bowel movement regular, no complaint gain of 11 lb	Patient's good general condition and youth favored a complete operation in one stage
Appendix injected slight amount of serous fluid terminal 12 in. of ileum inflamed slightly thickened, with edema of the mesentery and enlarged glands	Appendectomy, mesenteric gland excised for biopsy	Chronic obliterating appendicitis, acute nonspecific inflammation of lymph node	Small right pulmonary infarct on fifth day, elevated up on eleventh day, sutures removed on seventh day	8/12/34	11/10/34 bowel movement regular, no complaint gain of 6 lb	Early stage of regional ileitis with acute symptoms
Appendix inflamed, free serous fluid, terminal 5 in. of ileum inflamed slightly thickened, with edema of mesentery and enlarged glands	Appendectomy and culture of abdominal fluid	Subacute appendicitis, culture negative	Sutures removed on seventh day, uneventful recovery	8/13/34	12/10/34 bowel movement regular, no complaint gain of 5 lb x rays showed slight narrowing of terminal ileum	Early stage of regional ileitis with acute symptoms
Terminal 2 ft of ileum inflamed with very thick walls and obstruction to ileocecal valve, edema of mesentery with enlarged glands moderate amount of serous fluid	Ileocolostomy through right rectus incision between ileum 3 ft from ileocecal junction to transverse colon, no drainage (9/21/34)	Subacute nonspecific ileitis, with ulceration	Sutures removed on eighth day, uneventful recovery	Died 10/13/34		Collection developed in lumbar wound which was opened and drained condition seemed to progress satisfactorily until 10/14/34 when murmur developed, which rapidly advanced to uræmia and death
Ulceration and necrosis of wall of ileum, mesenteric glands beginning to suppurate	Through incision in right kidney, resection of 2 ft of terminal ileum, cecum and portion of ascending colon, cigarette drain (10/4/34) Blood transfusion 10/14/34		Infection of wound with faecal slough			
Terminal 10 in. of ileum and cecum inflamed and thickened with complete occlusion of ileocecal valve, free serous fluid, fistulous tract extending from stump of appendix to anterior abdominal wall marked distention of proximal end of small intestine	Fistulous tract excised circumferentially down to cecum, resection of terminal 14 in. of ileum, cecum and half of ascending colon, with ileocolostomy between ileum 2½ ft from ileocecal junction to transverse colon, Witzel enterostomy about 8 in proximal to anastomosis, no drainage	Chronic nonspecific ileitis with superimposed acute ulcerations complete occlusion of ileocecal lumen	Enterostomy tube removed on seventh day, sutures removed on eighth day, uneventful recovery	10/29/34	12/13/34 bowel movement regular, no complaint gain of 9 lb	Operation performed in one stage in spite of acute obstruction because of patient's good general condition, Witzel enterostomy assured success of the procedure
Appendix congested terminal 9 in. of ileum inflamed slightly thickened free serohemorrhagic fluid, with edema of mesentery	Appendectomy and biopsy of ileum	Subacute nonspecific ileitis, with mucosal hypertrophy chronic appendicitis	Sutures removed on seventh day, uneventful recovery	11/18/34	12/13/34 bowel movement regular, no complaint gain of 4 lb	Early stage of regional ileitis with acute symptoms
Appendix congested terminal 18 in. of ileum inflamed and somewhat thickened edema of mesentery and enlarged glands, no obstruction, moderate amount of serous fluid	Appendectomy and biopsy of ileum	Acute nonspecific ileitis chronic appendicitis	Sutures removed on eighth day, uneventful recovery	1/19/35	2/2/35 bowel movement regular, no complaint gain of 12 lb	Early stage of regional ileitis with acute symptoms



times only the surface epithelium is destroyed. There is a marked infiltration with polymorphonuclear cells, lymphocytes, plasma cells and fibroblasts. In some cases, foreign body giant cells are noted in considerable quantities, as a result of an inflammatory reaction around inclusion particles of foreign matter in the depth of the ulcers. The histologic observation of these cells plus the appearance on the serosa of small elevations discretely placed, simulating tubercles, is probably responsible for the classification of a great many of the cases in previous reports as instances of tuberculosis of the intestines.



Fig 5 (case 15) —High power magnification, showing the nodular form of cellular infiltration, with giant cells within the musculature

#### ROENTGEN OBSERVATIONS

Satisfactory roentgen examination of the ileum may be accomplished in two ways. One is by giving a barium sulfate meal early in the day and observing its progress frequently from the fifth until the ninth hour. The best results are obtained by following the progress of the meal fluoroscopically, with manual manipulation under the screen, and making roentgenograms at the times best indicated by the fluoroscopic examination. The other method is the giving of a barium sulfate enema

in 2 cases. The details of temperature, pulse rate and variations in the white blood cell count are given in table 1. In 7 cases simple appendectomy was performed, in 7, a one stage resection and in 3 a two stage resection. In all the cases but 1 there was a fairly consistent relationship between the extent of the lesion and the duration of symptoms.

Clinically, the condition can be divided into three stages. The first stage is characterized by a mild acute inflammation of the wall with edema noticeable, particularly at the mesenteric border of the intestine. The second stage is one in which the ulceration and the deposition of fibrous tissue in the wall have progressed to such a degree that restitution to normal is not possible. With a continuation of the inflammatory process, either stenosis or perforation or perhaps both occur and radical surgical intervention becomes inevitable. The third stage consists of second stage pathologic involvement presented for treatment either during the phase of acute obstruction or perforation or after a fistula has developed.

In the first stage the symptoms are those of acute appendicitis. There is a history of pain in the lower portion of the abdomen localized to the right side with nausea, vomiting and some elevation of temperature. Examination reveals a well nourished person, usually with tenderness and rigidity localized to the right lower quadrant and with rebound tenderness. In the second stage the usual diagnosis from the symptoms points toward an acute intestinal obstruction associated with an inflammatory process in the right lower quadrant. There is a history of previous constipation or diarrhea and previous attacks of pain in the right lower quadrant referable to lesser degrees of partial obstruction. During the acute attack of obstruction there are obstipation, nausea, vomiting, rapid pulse, a slight rise in temperature and leukocytosis. On examination the patient usually appears to be acutely ill and besides tenderness and rigidity in the right lower quadrant there is some degree of distention. Peristalsis may be visible abdominally, and a tumor may be palpable in the right lower quadrant. In the third stage the patient usually has a fecal or intestinal fistula as a result of or following previous appendectomy with some loss of weight, general weakness and abdominal cramps. Examination usually reveals one or more abdominal scars of previous operation with a fecal fistula.

#### PATHOLOGIC PICTURE

The appearance of the intestine in the early stage is that of a soggy, edematous mass which has a feeling that can be likened to that of sponge rubber. The mesentery is similarly involved. When squeezed the intestine is almost crepitant. The edema is best visible at the

summary of the cases in which cure resulted Table 5 is a summary of the cases in which death occurred either immediately or within the next few months after operation In addition to the tabulated cases there were 4 in which neither cure nor death had occurred at the time the report was made The data are given in table 6

TABLE 3—*Site of the Lesion in 126 Cases Reported in the Literature*

Site	Number of Cases	Author
Terminal portion of ileum	48	Coffen (J A M A 85 1303 [Oct 24] 1925), Crohn, Ginsburg and Oppenheimer <sup>1</sup> , Clute <sup>4</sup> , Rockey <sup>3</sup> , Harris, Bell and Brunn <sup>6</sup> , Colp <sup>8</sup> , Crohn <sup>9</sup> , Mock <sup>2</sup> , Erdmann and Burt <sup>14</sup> , Homan <sup>5</sup> and Hass <sup>10</sup> , Ladd <sup>7</sup> , Bissell (Ann Surg 99 957, 1934), Williams (Virginia M Monthly 60 728, 1934), DeCourcy, <sup>5</sup> Jackman <sup>18</sup> , Cushway (Illinois M J 66 525, 1934)
Ascending colon and cecum	13	Moschcowitz and Wilensky, <sup>13</sup> Eggers <sup>21</sup> , Peterson <sup>10</sup> , Brown, Bagen and Weber <sup>16</sup> , Lowen (Deutsche Ztschr f Chr 129 221, 1914), Korte (Arch f klin Chr 118 138 1921)
Sigmoid flexure	10	Proust <sup>1</sup> , Moynihan (Edinburgh M J 21 228, 1907), Robson (Brit M J 1 425, 1908), Dalziel (Brit M J 2 1068, 1913), Monserrat (Brit M J 2 63, 1907), Braun <sup>13</sup>
Cecum	8	Jeffries (J M A South Africa 2 184, 1928), Vock <sup>2</sup> , Nemilov (Arch f klin Chr 153 346, 1928), Korte, Tietze (Ergebn d Chir u Orthop 12 211 1920)
Cecum and terminal portion of the ileum	9	Dalziel, Moschcowitz and Wilensky <sup>13</sup> , Mock, <sup>2</sup> Erdmann and Burt, <sup>14</sup> Gordon <sup>10</sup> , Brown, Bagen and Weber, <sup>16</sup> Cushway
Jejunum	7	Dalziel, Harris, Bell and Brunn <sup>6</sup> , Brown, Bagen and Weber <sup>16</sup>
Ascending colon cecum and terminal portion of ileum	4	Erdmann and Burt <sup>14</sup> , Crohn <sup>9</sup> , Donchess and Warren (Arch Path 18 22 [July] 1934), Korte
Middle portion of the ileum	3	Dalziel
Transverse colon	3	Moynihan, Dalziel, Robson
Ascending colon	3	Robson, Moschcowitz and Wilensky <sup>13</sup>
Stomach	3	Mock <sup>2</sup>
Entire small intestine	2	Dalziel
Entire lower portion of the small intestine	1	Crohn <sup>9</sup>
Jejunum and ileum	3	Ladd <sup>7</sup> , Corr and Boeck <sup>11</sup> , Schapiro (J Mt Sinai Hosp 1 121 [Sept] 1934)
Omentum and secondary intestinal involvement	2	Proust, <sup>1</sup> Mock <sup>2</sup>
Splenic flexure and small intestine	1	Robson
Splenic flexure and stomach	1	Mock <sup>2</sup>
Splenic flexure	1	Moschcowitz and Wilensky <sup>13</sup>
Transverse colon and splenic flexure	1	Moynihan
Hepatic flexure	1	Mock <sup>2</sup>
Hepatic flexure and ascending colon	1	Mock <sup>2</sup>
Cecum and ileocecal valve	1	Golob (M J & Rec 135 390 1932)

A study of the aforementioned tables reveals the following facts The general mortality was 14 per cent Of the 65 cases in which resection was performed there was recurrence of the original lesion in spite of radical resection in 10, or 15 per cent In 6 of these a second operation resulted in cure, in 3 there was a fatal outcome after a second operation, and in 1 of the 10 further surgical procedure had not been carried out at the time of the report Simple side-tracking operations were performed in 15 cases and resulted in cure in 13 cases, in death in 1 case and in persistent external fistula in 1 case In 8 cases the early form of the lesion was encountered, and although no intestinal

ulcerations, there is formed a hobnail appearance of the mucosa, which in its exaggerated form looks like polyposis. As the lesion involves the ileocecal valve, this becomes hyperplastic, rigid and unyielding, finally developing into a stenotic membrane. The lesion is not confined to the mucosa. In the muscularis there is an inflammatory process accompanied by hyperplasia and fibrosis. In the earlier stages of the process the wall becomes markedly thickened, so that its diameter is several times the normal, as a result not only of hyperplasia but also of edema. Thus, the transverse diameter of the wall of the intestine at this time is much greater than normal. Simultaneously, however, the lumen of the bowel becomes smaller, and in extreme forms it may become almost completely obliterated (figs 2 to 5). Before the devel-



Fig 2 (case 15) —Specimen hardened and shrunk in solution of formaldehyde, showing (A) tremendous thickening of the intestinal wall in cross-section at the expense of the lumen, causing clinical acute obstruction, and (B) the area beyond the lesion, with normal mucous membrane and lumen

opment of the stenotic stage, that portion of the intestine which is proximal to the lesion is considerably smaller in caliber than the affected loop. When the stenotic stage develops instead of being smaller in diameter the proximal portion of the intestine becomes larger as a result of dilatation accompanying the obstruction. As the lesion progresses, the contraction of the fibrous tissue deposited in the wall during the stage of inflammation becomes manifest. The transverse diameter of the intestine becomes less than formerly, and the whole process assumes the appearance of a rubber hose. The appearance is characteristic at operation and even on roentgen examination no peristaltic movements

TABLE 4—Cases in the Literature in Which Surgical Intervention Caused a Cure  
—Continued

Authors*	Case No	Site of Lesion	Surgical Procedure
Crohn <sup>9</sup>	59	Terminal portion of ileum Ascending colon Hepatic flexure Sigmoid	(1) Appendectomy followed by progression of symptoms Multiple resections
	60	Terminal portion of ileum	Resection
	61	Terminal portion of ileum	Resection
Brown, Borgen and Weber <sup>10</sup>	62 to 68	Ileum	Side tracking (3), resection (4) (1 or 2 stages)
	69	Jejunum	Side tracking
	70 to 75		Side tracking (1) resection (5) (1 or 2 stages)
	76	Terminal portion of ileum	No intestinal operation (appendectomy)
Donchess and Warren	77	Cecum Ascending colon Terminal portion of ileum	} Resection
Jackman <sup>18</sup>	78	Terminal portion of ileum	Resection
	79	Terminal portion of ileum	Resection
Schapiro	80	Terminal portion of jejunum and upper portion of ileum	Resection
Cushway	81	Terminal portion of ileum and cecum	Resection
	82	Terminal portion of ileum	Resection

\* Reference to authors not mentioned in the text will be found in table 3

procedure was instituted, cure resulted (Proust,<sup>1</sup> Mock,<sup>2</sup> Rockey,<sup>3</sup> Clute,<sup>4</sup> DeCourcy<sup>5</sup>) In 6 other cases in which the early stage was observed at the primary operation and no intestinal procedure was instituted, there was marked progression of the intestinal disease, necessitating further operation In this group subsequent resection resulted in cures in 4 cases, death in 1 case and intractable fistula in 1 case (Harris, Bell and Brunn,<sup>6</sup> Ladd,<sup>7</sup> Colp,<sup>8</sup> Crohn,<sup>9</sup> Peterson,<sup>10</sup> Corr and Boeck<sup>11</sup>)

1 Proust, M R Tumeur para-intestinale [Rapport par Lejars], Bull et mem Soc de chir de Paris **33** 1158, 1907

2 Mock, H E Infective Granuloma, Surg, Gynec & Obst **52** 672 (March) 1931

3 Rockey, E W Thickening of Terminal Ileum with Mesenteric Adenitis in Children, Northwest Med **32** 145 (April) 1933

4 Clute, H M Regional Ileitis, S Clin North America **13** 561 (June) 1933

5 DeCourcy, J L Terminal Ileitis Simulating Acute Appendicitis (Case Report), J Med **15** 216 (June) 1934

6 Harris, F I, Bell, G H, and Brunn, H Chronic Cicatrizing Enteritis Regional Ileitis (Crohn), Surg, Gynec & Obst **57** 637 (Nov) 1933

7 Ladd, William, in discussion on Homans and Hass<sup>19</sup>

8 Colp, R Case of Nonspecific Granuloma of Terminal Ileum and Cecum, S Clin North America **14** 443 (April) 1934

9 Crohn, B B Broadening Conception of Regional Ileitis, Am J Digest Dis & Nutrition **1** 97 (April) 1934

10 Peterson, E Non-Specific Granuloma of Ileum, Ann Surg **97** 130 (Jan) 1933

11 Corr, P, and Boeck, W C Chronic Ulcerative Enteritis (Regional Ileitis), Am J Digest Dis & Nutrition **1** 161 (May) 1934

stage. Apparently the tendency toward perforation is counteracted by adhesions to neighboring viscera, the omentum or the parietal peritoneum, so that when ulceration occurs through all the coats of the small intestine, the discharge of the intestinal content is either into some other organ or out on the surface, but not into the free peritoneal cavity. Occasionally the perforation occurs into a walled-off area within the peritoneal cavity and results in an abscess, which as a rule is considered to have arisen from an appendicular inflammation. When such an abscess is drained subsequently, whether the appendix is

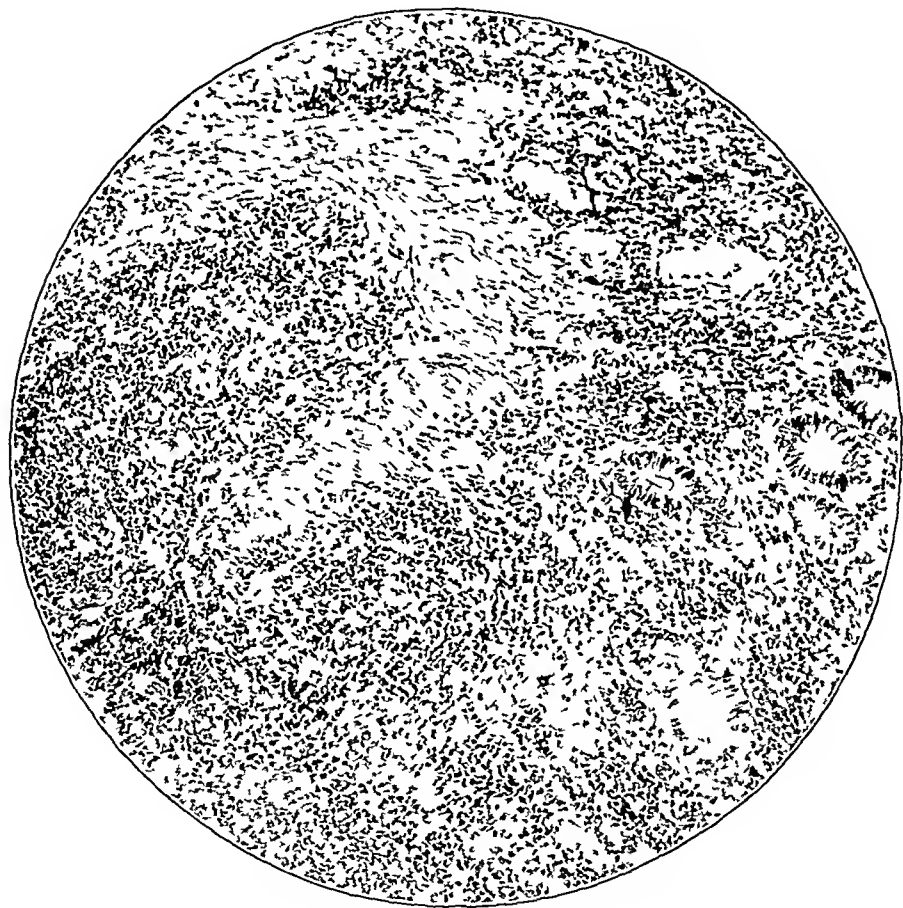


Fig 4 (case 15) —Section showing ulceration of the mucosa and cellular infiltration of the wall

removed or not, it gives rise to a chronic fistula, which cannot be closed by a simple method because of the underlying inflammatory disease of the intestine.

Microscopically, the sections show various degrees of acute, subacute and chronic inflammatory change throughout the wall of the intestine, particularly in the mucosa, where there is also marked destruction of an irregular type. In some instances the entire mucosa is gone, at other

thus that extensive involvement, recurrence of the lesion and jejunal involvement are unfavorable factors as far as prognosis as to life is concerned

A review of the reports of cases in which cure occurred revealed 54 instances of radical resection and 13 instances of side-tracking operations. There were 8 cases in which an early lesion was encountered in which surgical procedure was not performed on the intestine.

Following the publication of the paper of Crohn, Ginzburg and Oppenheimer<sup>17</sup> in 1932, a fair number of isolated cases, in groups of 1, 2 or 3, were reported in which the lesion in the terminal portion of the ileum was described and the condition was considered a definite disease entity (Crohn, Ginzburg and Oppenheimer,<sup>12</sup> Clute,<sup>4</sup> Jackman,<sup>18</sup> Colp<sup>8</sup>). However, other papers soon appeared in which the authors expressed the opinion that the disease in the terminal portion of the ileum was not especially different from similar inflammatory involvement of other portions of the intestine (Homans and Hass,<sup>19</sup>

TABLE 6—*Cases in the Literature with Improvement and Persistent Fistulas or Recurrence (with No Further Therapy at the Time the Case Was Reported)*

Author	Case No.	Site	Procedure	Result
Peterson <sup>10</sup>	1	Cecum ascending colon	Side tracking	Persistent fistula
Homans and Hass <sup>19</sup>	2	Terminal portion of ileum	Resection	Recurrent
	3	Terminal portion of ileum	Resection	Improvement
Ladd <sup>7</sup>	4	Lower portion of jejunum and terminal portion of ileum	Multiple resections	Improvement

Harris, Bell and Brunn,<sup>6</sup> Crohn<sup>9</sup>) The similarity of the lesion as it is described by various pathologists, regardless of the portion of the intestine involved, and the clinical course in the cases cited in the literature in which the pathologic process was not limited to the terminal portion of the ileum make us believe that the location in the terminal portion is merely more frequent than elsewhere but that the underlying disease is the same if regarded from the point of view of the pathologist. Clinically, the syndromes encountered are different according to the location of the pathologic process. Thus, the early stage of ileitis of the terminal portion gives the picture of irritation in the right lower quadrant of the abdomen associated with varying amounts of obstruction of the small intestine or of varying degrees of

<sup>18</sup> Jackman, W. A. Localized Hypertrophic Enteritis as Cause of Intestinal Obstruction, *Brit J Surg* **22** 27 (July) 1934

<sup>19</sup> Homans, J., and Hass, G. M. Regional Ileitis. Clinical Not Pathological Entity, *New England J Med* **209** 1315 (Dec 28) 1934

under roentgenoscopic control until the terminal portion of the ileum is filled to the required degree by reflux through the ileocecal valve. The large intestine is then emptied by defecation, and the ileum remains filled with the contrast fluid. Normally the final loop of the ileum rises up out of the pelvis toward the ileocecal valve. In the early stages of the disease, the earliest finding in this part of the ileum is an absence of variation in the diameter of the tube, denoting a degree of rigidity which parallels the amount of cicatrization. Segmentation and peristalsis are not noted. As the process progresses, a constant filling defect in this terminal portion of the ileum develops, the extent of which depends, of course, on the degree of stenosis. Still later, when the filling defect becomes great enough, it is replaced by a thin, irregular stringy shadow caused by the very small amount of contrast medium which has passed through the stenotic opening. This appears throughout the entire extent of the filling defect, running from the beginning of the lesion to its termination. With the progress of the stenosis, as low grade obstruction develops, there is dilatation of the proximal coils and a lagging of the opaque meal in the ileum for more than nine hours. Another roentgenographic characteristic is a more or less fixed position of the loop, so that where the rigidity of the tube with lack of peristalsis is noted or where the stringy trace of barium of the stenosed ileal lesion is seen it remains more or less fixed in relatively the same position on successive plates even after several days. Kantor pointed out the roentgenologic criteria for differential diagnosis from a filled appendix: the line of the right sacro-iliac synchondrosis, normal spasm of the ileum without organic circumscribed lesions, tuberculoma, stenosing sarcoma and ileal syphilis.

#### REVIEW OF THE LITERATURE

Nonspecific inflammatory disease of the intestinal tract has been known for many years. It has been reported as occurring in many portions of the gastro-intestinal tract. Table 3 is a compilation of reports on 126 cases, showing the various sites of occurrence of the lesion and giving the names of the authors. Many other cases have been mentioned in various papers, but histories were not given, so that the cases were unavailable for statistical study.

Of 62 reports in which the sex was stated, the lesion occurred in males 33 times and in females 29 times. The incidence according to age was as follows: first decade, 6, second decade, 10, third decade, 12, fourth decade, 15, fifth decade, 13, sixth decade, 6, and seventh decade, 5. These 67 cases were collected from reports in which the age was stated.

In the histories of 100 of the 126 collected cases the surgical therapy was clearly reported and the ultimate results were stated. Table 4 is a



The early lesion in many instances is spontaneously cured (in 6 cases in our series and in 8 in the literature) That there are many cases in which spontaneous cure has occurred without diagnosis or operation seems probable Therefore, conservatism in the management of the early lesion is indicated The therapeutic value of roentgen ray treatment is a moot question, the number of cases in which it was given being too small to allow of conclusions (Eggers,<sup>21</sup> 2 cases after side-tracking, Peterson,<sup>10</sup> 1 case, and ourselves, 4 cases) On the other hand, in 6 cases reported in the literature there was subsequent marked progression, necessitating radical surgical procedure Also, in 13 cases of advanced lesion a side-tracking operation resulted in cure This suggests the advisability of side-tracking in cases in which the process has advanced beyond the very early stage (In this connection, it must be remembered that the personal equation is an important factor in grading the stage of the lesion, since individual experience has not been very extensive)

With the moderately advanced lesion, the choice of procedure lies between a side-tracking operation and resection The desirability of eradicating a focus in which at this stage the chance for regression to normal is probably very slight favors resection as the procedure of choice If side-tracking is decided on, occlusion of the ileum proximal to the lesion is advisable

In cases of the advanced stage resection is indicated Whether it is performed in one or more stages depends on many factors If the condition is complicated by acute obstruction, one stage resection is to be avoided If the obstruction is of long standing, an enterostomy is the best immediate procedure This is subsequently followed by resection If the patient's condition warrants, the obstruction may be relieved by a side-tracking anastomosis Here, however, delay in proceeding with the resection is fraught with the danger of rapid progression of the lesion, necrosis and suppuration in the mesentery (Braun,<sup>13</sup> case 2) and possibly peritonitis from the perforation of such an abscess or even of the intestine itself The experiments on dogs with acute obstruction and the clinical experience of Holm<sup>22</sup> emphasize this point

With complicating fistulas the resection becomes more difficult The judgment of the operator and the extent of the lesion must determine the amount of intestine to be resected In our 2 cases only the small

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21 Eggers, Carl Non-Specific Granuloma of Ileum *Ann Surg* **97** 130 (Jan) 1933

22 Holm, C E Fate of the Sidetracked Loop of Ileum Following Lateral Anastomosis for Complete, Benign Obstruction, *Surg, Gynec & Obst* **56** 745 (April) 1933

TABLE 4—Cases in the Literature in Which Surgical Intervention Caused a Cure

Authors*	Case No	Site of Lesion	Surgical Procedure
Proust <sup>1</sup>	1	Colon	Multiple resection
	2	Sigmoid flexure	Incision and drainage (no operation on intestine)
Морниган	3	Transverse colon and splenic flexure	Side tracking
Robson	4	Sigmoid flexure	Colostomy
	5	Small intestine	Ileostomy
	6	Transverse colon	Side tracking
	7	Ascending colon	Side tracking
	8	Splenic flexure and small intestine	Double side tracking
Dalziel	9	Jejunum	Resection
	10, 11	Cecum and ileum (2 cases)	} Type not stated but surgical procedure was carried out
	12	Sigmoid flexure	
	13	Transverse colon	
	14	Middle portion of ileum	
Coffen	15	Terminal portion of ileum	Multiple resection (2) (recurrent intestinal obstruction)
Mosehowitz and Wilensky <sup>13</sup>	16	Cecum and ileum	Multiple resection (3) (recurrent intestinal obstruction)
	17	Cecum and ascending colon	Resection
Jeffries	18	Cecum	Side tracking
Moek <sup>2</sup>	19	Sigmoid flexure	No operation on intestine
	20	Pyloric mass	Resection
	21	Gastro intestinal mass	Resection
	22	Splenic flexure and stone	Resection (multiple fecal fistula)
	23	Terminal portion of ileum and cecum	Resection
	24	Ileum	Resection
Golob	25	Cecum and cecal valve	Resection
Crohn Ginzburg and Oppenheimer <sup>17</sup>	26	Terminal portion of ileum	Resection (exact operation for individual case not given)
	27, 38	Terminal portion of ileum	
Erdmann and Burt <sup>14</sup>	39	Ileocecal junction	Resection
	40	Terminal portion of ileum	Resection
	41	Cecum, ascending colon, terminal portion of ileum	Resection
Clute <sup>4</sup>	42	Terminal portion of ileum (mesenteric abscess)	Incision and drainage of abscess (no operation on intestine)
	43	Terminal portion of ileum	Side tracking
Gordon <sup>15</sup>	44	Ileocecal mass	Resection
Eggers <sup>21</sup>	45	Cecum and ascending colon	Side tracking (transsection of small intestine)
	46	Terminal portion of ileum	(1) side tracking (multiple operations) transsection of small intestine (2) For obstruction by a band of adhe signs
Rockey <sup>3</sup>	47	} Terminal portion of ileum	{ No intestinal operation
	48		
	49		
	50		
Harris Bell and Brunn <sup>6</sup>	51	Terminal portion of ileum	(1) Drainage for appendicitis (2) Resection of terminal portion of ileum ascending colon and cecum
Homans and Hass <sup>19</sup>	52	Terminal portion of ileum	Resection
Ladd <sup>7</sup>	53	Lower portion of jejunum	Multiple resection
		Terminal portion of ileum	{ (1) Exploratory laparotomy and biopsy (2) Resection (3) Resection
	54	Terminal portion of ileum	
	55	Terminal portion of ileum	
Bissell			Multiple operations (1) Resection (Mikulicz) (2) For intestinal obstruction (bands)
Colp <sup>8</sup>	56	Terminal portion of ileum	Resection
Williams	57	Terminal portion of ileum	(1) Appendectomy (2) resection
	58	Small intestine	Resection

# EFFECT OF INFLAMMATION ON THE EPIPHYSES

R A Y JOHNSTON, M D

LONDON, CANADA

The known and commonly described infections which occur in human beings at the epiphysis or at its union with the diaphysis are as follows

A Acute osteomyelitis

B Chronic involvement, associated with tuberculosis, syphilis, undulant fever (rare) or actinomycosis (rare)

C Gradual necrosing lesions of bone the etiology of which is disputed

- 1 Kohler's disease of the tarsal navicular bone, 2 Freiberg's disease of the heads of the metatarsal bones, 3 Kienbock's disease of the carpal semilunar bone and many other bones, 4 Koenig's osteochondritis dissecans of the medial condyle of the femur, 5 apophysitis of the os calcis (Sever), 6 aseptic necrosis of the head of the femur, the radius, the humerus or the distal epiphysis of the femur, 7 Osgood-Schlatter's disease of the tibial tubercle, 8 Legg's or Calve-Perthes' disease, osteochondritis juvenilis

In this paper it would be impossible to deal with this great variety of diseases about which so much has been contributed by clinicians, surgeons, roentgenologists and research workers of this and other countries, so I am limiting myself to the subject of acute osteomyelitis

The interest that has been shown in the recent adjuncts to the treatment of osteomyelitis (Orr's<sup>1</sup> method and Dolman's staphylococcus serum<sup>2</sup> during the acute stage and the various procedures for balancing the length of shortened extremities (Putti's,<sup>3</sup> Abbott's<sup>4</sup> and

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From the Division of Orthopedic Surgery of the Department of Surgery of the University of Western Ontario

Read before the Section on Surgery at the Eighty-Sixth Annual Session of the American Medical Association, Atlantic City, N J, June 13, 1935

1 Orr, H W Treatment of Osteomyelitis by Drainage and Rest, *J Bone & Joint Surg* **9** 733, 1927

2 Dolman, C E Staphylococcus Antitoxic Serum in the Treatment of Acute Staphylococcal Infections and Toxemias, *Canad M A J* **30** 601 (June) 1934

3 Putti, V Operative Lengthening of the Femur, *Surg, Gynec & Obst* **58** 318 (Feb) 1934

4 Abbott, L C The Operative Lengthening of the Tibia and Fibula, *J Bone & Joint Surg* **9** 128 (Jan) 1927

Fecal fistula occurred in 9 cases (Braun,<sup>12</sup> Moschcowitz and Wilensky,<sup>13</sup> Mock,<sup>2</sup> Erdmann and Burt,<sup>14</sup> Gordon,<sup>15</sup> Crohn,<sup>9</sup> Corr and Boeck,<sup>11</sup> Brown, Bargaen and Weber<sup>16</sup>) exclusive of the cases observed in Mount Sinai Hospital, reported on by Crohn, Ginzburg and Oppenheimer,<sup>17</sup> who did not mention the percentage of occurrence. A review of the fatal cases revealed the following: In 3 the condition was recurrent after previous resection, in 4 the jejunum was extensively involved, and in 5 there was extensive intestinal involvement: the entire intestine being involved in 2, the entire lower portion of the small intestine in 1 and extensive portions of the jejunum in 2. We may predicate from

TABLE 5—Cases in the Literature in Which Death Followed Surgical Procedure †

Authors*	Case No	Site	Procedure
Braun <sup>12</sup>	1	Sigmoid flexure	Multiple resection (recurrent)
Dalziel	2	Whole intestine	No operation on intestine
	3	Whole intestine	No operation on intestine
Moschcowitz and Wilensky <sup>13</sup>	4	Ascending colon and small intestine	Multiple resection (recurrent) resection
Mock <sup>2</sup>	5	Stomach	Resection
Erdmann and Burt	6	Terminal portion of ileum Ascending colon	Multiple resection (recurrent) Resection (terminal portion of ileum and ascending colon)
Harris, Bell and Brunn <sup>6</sup>	7	Terminal portion of ileum	Resection
	8	Jejunum	Resection
Crohn <sup>9</sup>	9	Whole lower portion of intestine	Resection
Corr and Boeck <sup>11</sup>	10	Terminal portion of ileum and jejunum (extensive involvement)	Side tracking (at previous operation of app) bowel lesion not advanced at time of side tracking, extensive involvement
Brown, Bargaen and Weber <sup>16</sup>	11	Jejunum	Procedure not stated but no resection done
	12	Jejunum (extensive involvement)	Closure of fistula
	13	Ileum	
Cushway	14	Terminal portion of ileum Cecum	Laparotomy

\* Reference to authors not mentioned in the text will be found in table 3.

† Factors influencing mortality were: recurrence after previous operation (3 cases), jejunal involvement (4 cases), and extensive involvement (5 cases).

12 Braun, H. Ueber entzündliche Geschwülste am Darm, Deutsche Ztschr f Chir **100** 1, 1909

13 Moschcowitz, Eli, and Wilensky, A. O. Nonspecific Granulomata of Intestine, Am J M Sc **166** 48 (July) 1923

14 Erdmann, J. F., and Burt, C. V. Non-Specific Granuloma of Gastro-Intestinal Tract, Surg, Gynec & Obst **57** 71 (July) 1933

15 Gordon, Donald. Non-Specific Granuloma of Ileum, Ann Surg **97** 130 (Jan) 1933

16 Brown, P. W., Bargaen, J. A., and Weber, H. M. Regional Enteritis, Proc Staff Meet, Mayo Clin **9** 331 (May 30) 1934

17 Crohn, B. B., Ginzburg, L., and Oppenheimer, G. Regional Ileitis, J A M A **99** 1323 (Oct 15) 1932

Starr<sup>8</sup> stressed the presence of a finger point of exquisite tenderness corresponding to the site of the epiphyseal line, and I have always found it a most reliable sign. It is found by gentle testing in a line commencing above and working down toward the joint on the surface of the skin over the side of the extremity nearest the pathologic condition. No doubt exists about the exquisite tenderness of this point when found, and its presence is a great aid in making an early diagnosis.

In addition to these local findings there are usually fever, with a temperature of from 102 to 103 F or more, and increase of the pulse

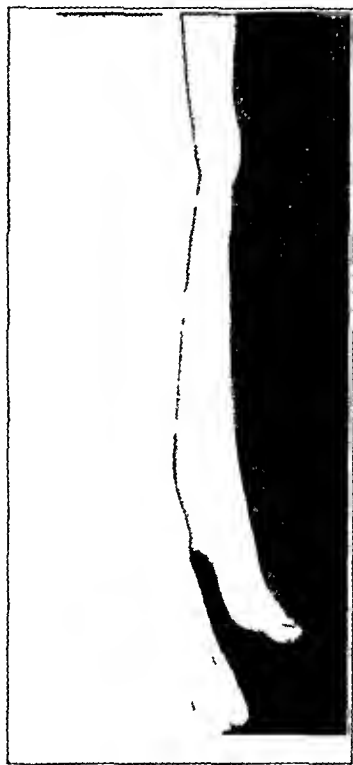


Fig 2—Acute osteomyelitis of three days' duration affecting the upper end of the right tibia of a 14 year old boy. Note the swelling of the limb.

rate to 120 or 140. The leukocyte count is definitely increased, the number varying in my series from 12,000 to 55,000 per cubic millimeter.

In this series I found that in several cases the condition had been diagnosed rheumatic fever and treated as such even after multiple foci had developed. The early swelling of an acute rheumatic joint and the fact that more than one joint is usually involved in rheumatic fever should aid in distinguishing this condition from acute osteomyelitis.

<sup>8</sup> Starr, Clarence L. Acute Infections of Bone, in *The Robert Jones Birthday Volume*, New York, Oxford University Press, 1928, p. 183.

severity of diarrhea, depending on the stage of the disease. Involvement of the sigmoid flexure presents the picture characteristic of inflammatory or obstructive disease of the large intestine. A lesion of the jejunum or the upper portion of the ileum gives the picture of inflammatory or obstructive disease of the small intestine. It is possible that the greater frequency of ileal involvement may be due to greater susceptibility of this portion of the intestinal tract to infection as is noted particularly in children by the development of mesenteric adenitis to a greater extent in the mesentery draining the terminal portion of the ileum than elsewhere in the intestinal tract.

*Etiology*—For a theoretical discussion on etiology reference should be made to the papers of Mock<sup>2</sup> and Ginzburg and Oppenheimer.<sup>20</sup> Because of the cicatrizing tendencies and the possible similarity to cicatrizing tendencies found in the rectum in cases of lymphogranuloma inguinale, we carried out the Frei test with negative results in 4 cases in which resection was performed and also in 2 cases in which resection was not done.

#### DIAGNOSIS

We should like to emphasize again the steps that must be taken to make the diagnosis. To begin with, any case in which there are symptoms of inflammatory intra-abdominal disease with peritoneal irritation as well as symptoms of varying degrees of intestinal obstruction must be considered as possibly an instance of regional ileitis. Long continued duration of symptoms is characteristic in many of these cases although occasionally the clinical course is short. We stress the importance of the roentgen findings, particularly as regards the use of the barium enema. The barium meal may also be used but to less advantage when the lesion is in the terminal portion of the ileum. It will be of much greater importance if the lesion is in the upper portion of the intestine. Serial plates must be studied to establish the diagnosis. General constitutional symptoms characteristic of inflammation of the intestinal tract such as fever, leukocytosis, increase in the pulse rate, etc., while present, offer little differential diagnostic aid.

#### TREATMENT

A review of the collected literature as well as of our own cases establishes certain guides for therapy.

The condition may be subdivided into three types: (a) the early lesion, (b) the moderately advanced but not obstructive lesion, and (c) the advanced stenotic or fistulous process.

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<sup>20</sup> Ginzburg, L. and Oppenheimer, G. D. Non-Specific Granulomata of the Intestines. Inflammatory Tumors and Strictures of the Bowel. *Ann Surg* 98: 1046 (Dec.) 1933.

the diagnosis of cellulitis had been made, however, this was made after the infection had existed for several days and perforation of the cortical bone had taken place. The presence of cellulitis draws attention to the fact that this condition was a complication and not the cause of the original infection. Primary cellulitis may be distinguished by the early swelling and redness which it causes and also by the fact that the pain and toxemia are not so marked as in acute osteomyelitis.

Acute septic arthritis, which like cellulitis may be a later complication of acute osteomyelitis, must also be distinguished when it occurs as a primary condition. The mono-articular character of the lesion is a troublesome diagnostic point, but the inflammatory demonstration is



Fig 4—*A* shows the femur of a rabbit which died eighteen hours after being inoculated with a broth culture of *Staph aureus* from the patient whose femur is shown in figure 3. The lower epiphysis was separated. *B* shows the epiphysis of the rabbit separated by the acute inflammatory process.

limited to the articulation, and aspiration of the joint will settle any question of doubt which may arise.

The history of trauma may cause some doubt as to the diagnosis of the lesion, but the examination and the presence of fever, toxemia and leukocytosis will reveal the true nature of the lesion.

I have produced acute osteomyelitis in the long bones of young rabbits by injection into the blood vessels<sup>9</sup> of 0.5 cc. of a broth culture of

<sup>9</sup> Kistler, Gene. Sequence of Experimental Infection of the Femur in Rabbits, *Arch Surg* 29:589 (Oct) 1934.

intestine was resected, the openings into the sigmoid flexure and cecum being closed by purse-string sutures. Both operations were carried out in one stage. Here also it may be advantageous to divide the procedure into two stages by a preliminary side-tracking operation.

#### SUMMARY

We have presented an analysis of our 17 cases of nonspecific inflammatory disease of the ileum and have analyzed the condition in 100 cases reported by others. From this study we have made generalizations regarding diagnosis, prognosis and therapy.



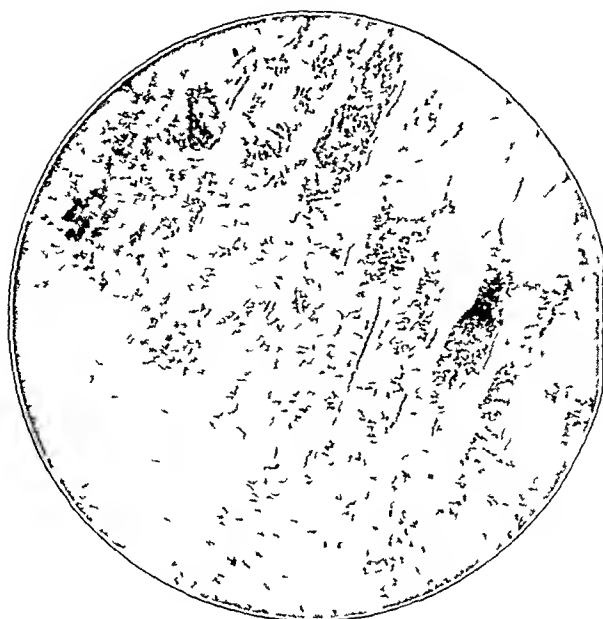


Fig 6—Photomicrograph (low power) showing experimentally produced osteomyelitis at the lower end of the femur in an 8 week old rabbit

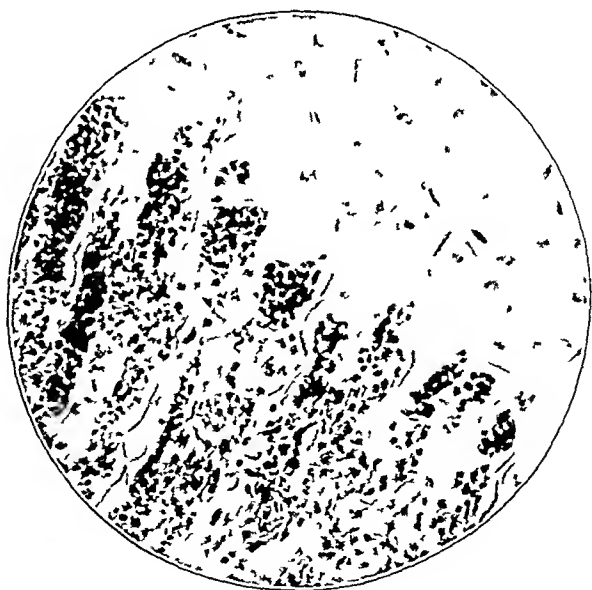


Fig 7—Photomicrograph (high power) showing the junction of the diaphysis and epiphysis. Note the acute inflammatory reaction on the diaphyseal side of the epiphyseal line

Phemister's<sup>5</sup> method) during the later stages of deformity has to some extent obscured the necessity for early diagnosis and immediate adequate surgical treatment as advocated by Starr.<sup>6</sup>

The primary pathologic change of acute osteomyelitis appears at the diaphyseal side of the epiphyseal cartilage, probably as an infective embolus, and produces a septic infarct the same as would occur in any other tissue.

The lodging of an embolus or the collection of a group of organisms in this particular location has been accounted for anatomically<sup>7</sup> by the arrangement of the blood vessels and also by the fact that the direct supply of blood at the site consists of terminal arteries (fig 1).

A clinical picture is produced which nearly always is acute and characteristic. The patient, more often a boy from 9 to 14 years of age, complains of acute pain near the end of one of his long bones frequently

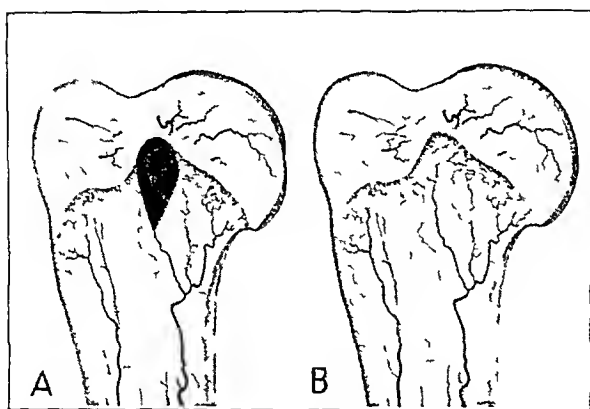


Fig 1—A shows the location of the early lesion of acute osteomyelitis in relation to the supply of blood of the epiphyseal line. B shows the vascular supply of bone (after Harris).

the lower end of the femur or the upper end of the tibia. A history of trauma is sometimes present, and often a scrutiny of the affected extremity reveals the site of a recently infected blister, callus or cutaneous wound or the presence of some recent cutaneous infection, or the history of a recent cold or minor ailment may be obtained. The extremity is held in a position of flexion, and although swelling is not an early sign it soon appears and is best noted by a comparison with the opposite extremity (fig 2).

<sup>5</sup> Phemister, D. B. Operative Arrestment of the Longitudinal Growth of Bone in the Treatment of Deformities. *J. Bone & Joint Surg.* **15**: 1 (Jan.) 1933.

<sup>6</sup> Starr, C. L. Acute Hematogenous Osteomyelitis, *Arch. Surg.* **4**: 567 (May) 1922.

<sup>7</sup> Harris, H. A. The Vascular Supply of Bone with Special Reference to the Epiphyseal Cartilage, *J. Anat. & Physiol.* **64**: 1, 1930.

tion was for adequate drainage. This, I think, accounts for the high percentage of patients showing epiphyseal involvement and interference with growth, but on the other hand my conservative type of operation on the acutely ill patients and on those whose disease was in the early stages accounts for the low mortality.<sup>11</sup>

Pyrah and Pain<sup>10</sup> reported 52 deaths in 176 cases of acute osteomyelitis in which treatment was primarily by guttering, while I have treated 73 patients with involvement of 105 bones, with only 1 death by using more conservative treatment (table 2). Pyrah and Pain ended

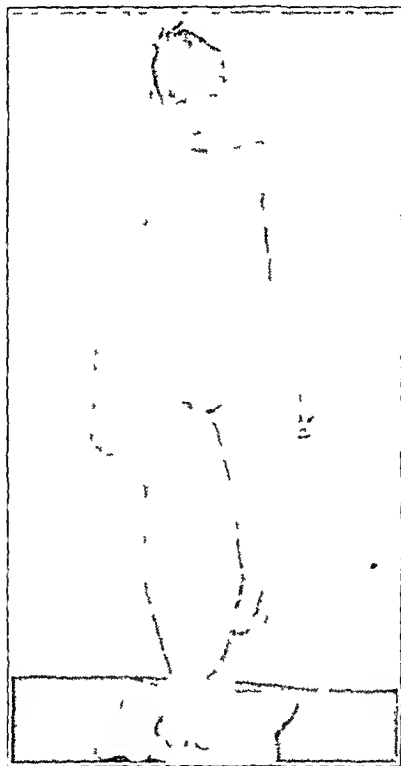


Fig. 9—A marked bowleg deformity in a patient who had acute osteomyelitis with metastases due to destruction of the medial part of the epiphyseal line of the upper end of the tibia and unequal growth and unsupported weight bearing.

their discussion by pointing out the necessity for a more conservative type of operation early in the disease.

A study of this series of cases of acute osteomyelitis and a comparison with the results of various methods of treatment reported in the literature shows that acute osteomyelitis is a very grave disease. The analysis of 262 cases with 71 deaths reported by Pyrah and Pain<sup>10</sup> in England showed a mortality of 27.1 per cent. In addition, a great many

<sup>11</sup> Ramsay, G. A. Personal communication.

However, there is an increase of synovial fluid in acute osteomyelitis when the lesion has developed, but at this stage the infection is definitely in the bone and is not articular

In a number of my cases in which the inflammation involved the upper end of the femur, humerus, scapula, pelvis and tarsal bones,

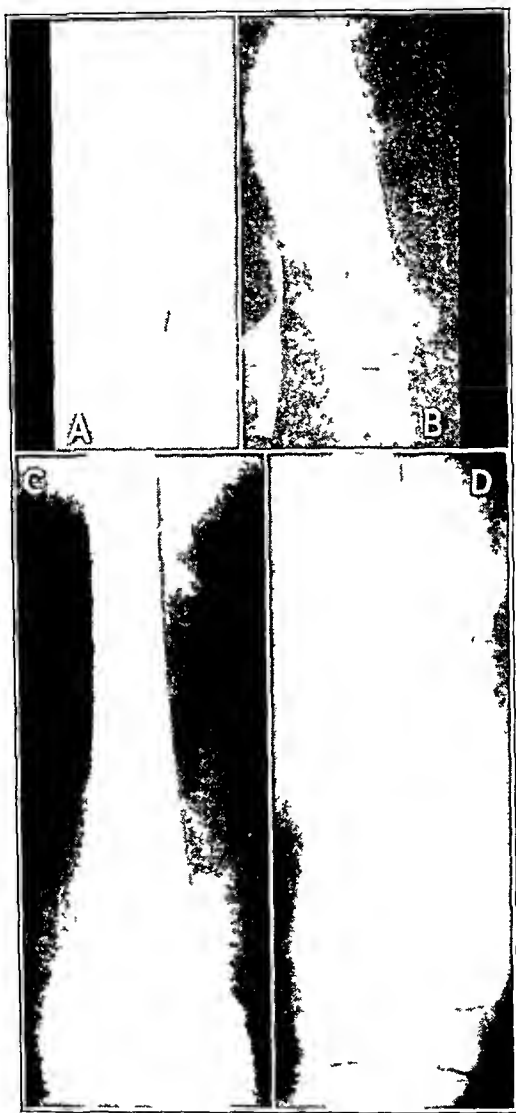


Fig 3—*A*, an early stage of osteomyelitis of the lower end of the femur. Roentgenograms showed no osseous changes. The high riding patella suggests an increase of synovial fluid in the knee joint. *B*, lateral view of the bone. Note the perforation of the cortex just above the epiphyseal line posteriorly. *C*, roentgenogram of the bone twelve days later showing the misplaced drill holes and the inflammatory process progressing just above the epiphyseal line. *D*, the same bone, showing a section of cortex removed but not near enough to the epiphysis to allow free drainage. There is more destruction of the lower end of the diaphysis than is seen in *A*.

Bowleg and knock knee caused by arrest of either the inner or the outer half of the epiphyseal line of the lower end of the femur or of the upper end of the tibia occurred several times. Remarkable improvement

TABLE 1—*A Statistical Study of Acute Hematogenous Osteomyelitis Treated by the Surgical Service of the University of Western Ontario (1926-1935)*

Bones Involved	No of Cases	Aver age	Sex	Side	End*	Meta static Involvement	Arrest of Growth with Epiphyseal Involvement	No Arrest Epiphysis Intact	Not Traced	Too Recent	Died
Femur	38	11.5	M 27 F 11	R 20 L 28	U 10 L 28	8	18	16	3	1	1
Tibia	34	11	M 22 F 8	R 20 L 14	U 18 L 12	4	15	14	3	2	0
Humerus	10	9	M 3 F 4	R 6 L 4	U 3 L 7	3	5	2	2	1	0
Pelvis	6	9	M 3 F 3	R 3 L 3		2	3	2	0	1	0
Ulna	5	10	M 3 F 2	R 4 L 1	U 0 L 5	5	3	2	0	0	0
Os calcis	4	10	M 2 F 2	R 1 L 3		3	4	0	0	0	0
Radius	2	7.5	M 1 F 1	R 2	L 2	1	1	1	0	0	0
Scapula	2	5	M 1 F 1	R 1 L 1		2	1	0	0	1	0
Clavicle	1	12	F 1	R 1		1	0	1	0	0	0
Fibula	1	16	M 1	R 1	L 1	1	0	1	0	0	0
Sternum	1	19	M 1	Body		1	0	1	0	0	0
Skull	1	11	M 1	Frontal		1	0	1	0	0	0
Totals	105	9.5	M 65 F 33	R 58 L 45	U 31 L 44	32	50	41	8	6	1

\* U indicates upper, L, lower

TABLE 2—*Analysis of the Cases Listed in Table 1*

Total number of patients	73
Total number of bones involved	105
Number of bones showing interference with growth	50*
Number of bones showing no interference with growth	41
Number of cases in which patient was not traced	8
Number of cases too recent for opinion	6
Number of deaths	1
Percentage of bones showing involvement of growth	55.5

\* Two bones showed longitudinal overgrowth

has occurred in some of these cases by the patient's wearing Thomas walking calipers and relieving the site of deformity of the strain of bearing weight and using a strap

*Staphylococcus aureus*, obtained from patients in the early stages of acute osteomyelitis, and I have recovered the organism again, uncontaminated, from the epiphyseodiaphyseal joint of the infected bone. The macroscopic and microscopic examination of these specimens shows the type of lesion which occurs in acute osteomyelitis caused by *Staph aureus* and has a definite bearing on the type of surgical treatment that should be instituted (fig 3).

The question of the type of operation is one of great importance. All methods consist of exposure of the infected bone. The site of the epiphyseal line should be located. The fluoroscope is of aid in this, and the approximate location of the line can be marked on the surface of the skin. The incision should extend to this line, and the epiphyseal line should be identified. Due regard should be paid to the integrity of the capsule of neighboring joints, and a consideration of the attachment of tendons and ligaments will serve as a guide to the exposure of the

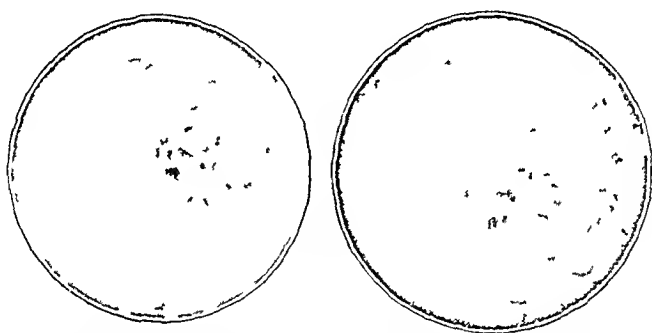


Fig 5—Pure growth of *Staph aureus* on blood agar plates. A is from the patient whose tibia is shown in figure 2, B, from the rabbit.

epiphysis. The periosteum should be incised in a linear direction to the epiphyseal line. Then the treatment of the bone itself is to be considered.

In early cases the location of the pathologic condition is best reached by the drilling of obliquely placed holes through the cortex of the bone to the epiphysis (fig 8).

Stall<sup>6</sup> advised simple periosteal incision in cases in which pus is found under the periosteum. If no pus is found, the bone should be drilled or trephined obliquely to the epiphyseal line. This procedure has many advantages, it is a fairly conservative procedure compared to the removal of a large segment of the cortex or to guttering the bone or diaphysectomy, and it allows drainage. Also bacteriologic studies can be made of the fluid and debris which come from the drilled holes.

Young patients suffering from the toxemia of acute osteomyelitis do not withstand severe operations, and a comparison of the mortality among a series of patients treated by extensive guttering as compared

performed at the proper point in the affected bone. His insistence on the classic principles is most worth while. If he approaches too close to the diaphyseal line of the epiphysis with the drill holes, perhaps it is possible to explain part of his large incidence of arrest in growth by damage to the diaphyseal cartilaginous cells in the same way that Dr. Compere explained arrest of growth following fractures. My experience with failure in growth following osteomyelitis has been more extensive than his. In the cases of failure in growth Dr. Johnston did not distinguish between those in which he operated himself and those in which less well informed surgeons operated.

DR. J. DEWEY BISGARD, Omaha. Dr. Johnston should be congratulated on the low mortality rate that he has had in cases of acute osteomyelitis. His unusually high incidence of disturbance in growth, I believe, can be explained by the fact that he carries the operation very close to the epiphyseal cartilage and into the juxtocartilaginous portion of the diaphysis, where longitudinal growth takes place. However, the deformities resulting from disturbance in growth constitute rather a small price to pay for the very low mortality rate that he has had in his series of cases.

DR. R. A. Y. JOHNSTON, London, Canada. Dr. Kidner mentioned that there is no doubt that those drill holes placed too close to the diaphyseal line of the epiphysis arrested growth. I wished to emphasize the necessity for placing them there. In practical cases, one does not try to go more than to the second or third drill hole or very far into the diaphyseal end of the bone. The incidence of deformity in the series I presented and comparison of the mortality in this series with that in a series of 262 cases in England that were reported in the *British Journal of Surgery* in April 1933, wherein 176 children with acute osteomyelitis were treated by the primary guttering operation and 52 per cent died, indicate, I believe, the practicality of my procedure. I allow supported weight bearing when the pathologic process has become quiescent, and as Dr. Ramsay, the director of our clinic, was trained by the Liverpool School, we sometimes persist with supported weight bearing. A study of the percentage of arrests of growth in the femur and the tibia in this series would indicate that continued protection does not protect against epiphyseal deformity.

to a series treated primarily by the more conservative drilling favors the conservative treatment<sup>10</sup>

The progress in a case of acute osteomyelitis is demonstrated in figures 5, 6, 7 and 8A, showing various changes which occur in the bone when the region of the end of the diaphysis is not adequately drained and emphasizing the necessity of draining the bone close to the epiphyseal line. The integrity of the epiphysis is a remarkable feature and supports the idea of its having a different blood supply than the diaphysis.<sup>7</sup> The fundamental principle of treatment is to give early and adequate drainage as close to the site of inflammation as possible, without injuring the growing end of the diaphysis more than necessary. This calls for carefully planned incision, exposure of the bone which shows

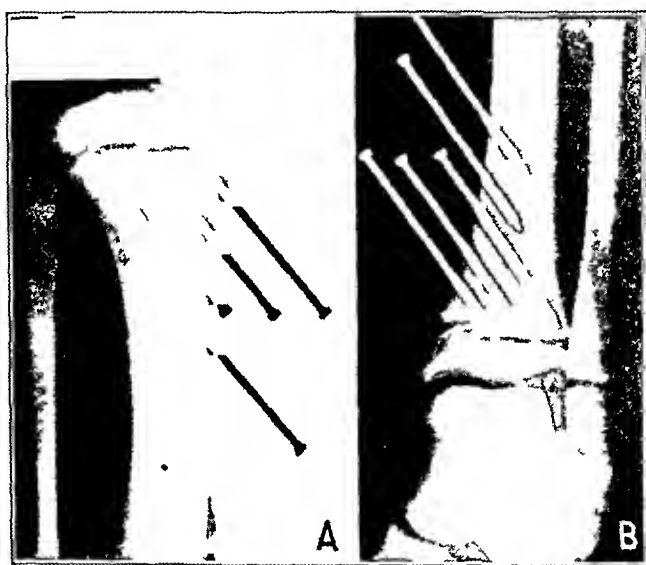


Fig 8—A shows drill holes placed obliquely to the epiphyseal line at the upper end of the tibia of a 7 year old boy. Two inch brads have been placed in the holes to afford contrast, B shows obliquely placed drill holes at the lower end of the tibia of the same patient. The holes would drain the cancellous bone at the end of the diaphysis, the site of the early pathologic condition of acute osteomyelitis.

the location of the epiphyseal line and careful opening of the periosteum and cortex of the bone without splintering or tearing the bone either toward the epiphysis or in the shaft. The drill fulfils these obligations and is always used by me in primary treatment of patients in whom the disease is in the early stage and those who are acutely ill. All cases are not diagnosed early, and many patients have reported to me when the suppurating process had become chronic and when the immediate indica-

10 Parah, L. N., and Pam, A. B. Acute Infective Osteomyelitis. A Review of Two Hundred and Sixty-Two Cases, *Brit J Surg* 20: 590 (April) 1933.



of these sections was placed flat and roentgenographed in the superior-inferior plane. After this, one or more portions removed from the middle third of the specimen were fixed in Helly's solution,<sup>1a</sup> decalcified in 5 per cent nitric acid, embedded in paroxylin (cellosum) and stained with hematein and eosin.

#### DEVELOPMENT OF THE SYMPHYSIS PUBIS

There has been a large amount of embryologic and anatomic work on this question.<sup>2</sup> The investigations have been carried out in man and in many species of animals. The results of such studies and the more or less accepted anatomic facts can be briefly summarized. Each pubic bone is derived from a center of ossification developing in cartilage. The cartilage plates meet in the midline of the body to form the symphysis pubis. Anteriorly, undifferentiated mesenchyme derived from the anterior ligament binds the two cartilage plates. This mesenchymal

#### *Age Groups and Sex Groups Represented by the Specimens Studied*

Age, years	Males	Females		Specimens
		Nulliparas	Multiparas	
0-5	4	3		7
6-10	2	3		5
11-20	6			6
21-30		2	1	3
31-40	7	3	2	12
41-50	7	2	3	12
51-60	8	7	4	19
61-70	5	2	2	9
71-80	2			2

tissue can be transformed into hyaline cartilage, in fact, this regularly occurs in some animals. In adult rats, however, there is no intervening tissue in the midline between the cartilaginous elements of the pubic

1a Helly's solution consists of potassium bichromate, 2.5 Gm., mercury bichloride, 5 Gm., and water, 100 cc. Add to 90 cc of this solution 10 cc of a 40 per cent solution of neutral formaldehyde solution, U.S.P., just prior to the fixation of the tissues.

2 Barlow, M. Peculiarities of the Pelvis in the Cow. *Month J. M. Sc.* **18**: 83, 1854. Humphry, G. M. A Treatise on the Human Skeleton, Cambridge, Macmillan & Co., 1858. Flower, W. H. Osteology of the Mammalia. London, Macmillan & Co., 1885. Bardeen, C. Studies of the Development of the Human Skeleton, *Am. J. Anat.* **4**: 265 (May) 1904-1905. Franz, K. Zur Entwicklung des knöchernen Beckens nach der Geburt, *Beitr. z. Geburtsh. u. Gynäk.* **13**: 12, 1908-1909. Adair, F. L. The Ossification Centers of the Foetal Pelvis, *Am. J. Obst. & Gynec.* **78**: 175 (Aug.) 1918. Dorland, W. A. N., and Hubeny, M. J. The X-Ray in Embryology and Obstetrics, London, Henry Kimpton, 1926. Dawson, A. B. Further Studies on the Epiphyses of the Albino Rat Skeleton, with Special Reference to the Vertebral Column, Ribs, Sternum and Girdles, *Anat. Rec.* **34**: 351 (Feb.) 1927.

patients go on for long periods of time with chronic discharging sinuses and acquire various degrees of lardaceous disease, and many are left with permanently damaged epiphyseal cartilage, which causes unequal length of extremities and various angular deformities such as bowleg and knock knee (figs 8B, 9 and 10)

Phemister<sup>5</sup> drew attention to the effect of injury and inflammation on the epiphysis and to the various deformities which may result. He advised operative arrest of the epiphyseal growth to balance the length of unequal extremities and to cure angular deformities at joints caused by unequal growth.



Fig 10—A marked knock knee deformity in a patient with a late stage of osteomyelitis of the upper end of the tibia, due to destruction of the lateral portion of the epiphyseal line and unequal growth.

I became interested in this type of deformity in osteomyelitis and have analyzed this series of cases to ascertain in what percentage the epiphyseal growth is interfered with by the inflammatory process (tables 1 and 2).

I found many instances of shortening of the femur and the tibia, one case of osteomyelitis of the upper end of the femur having caused shortening of the leg of  $4\frac{1}{2}$  inches (11.4 cm) and one of the upper end of the tibia having caused shortening of  $2\frac{1}{2}$  inches (6.3 cm).

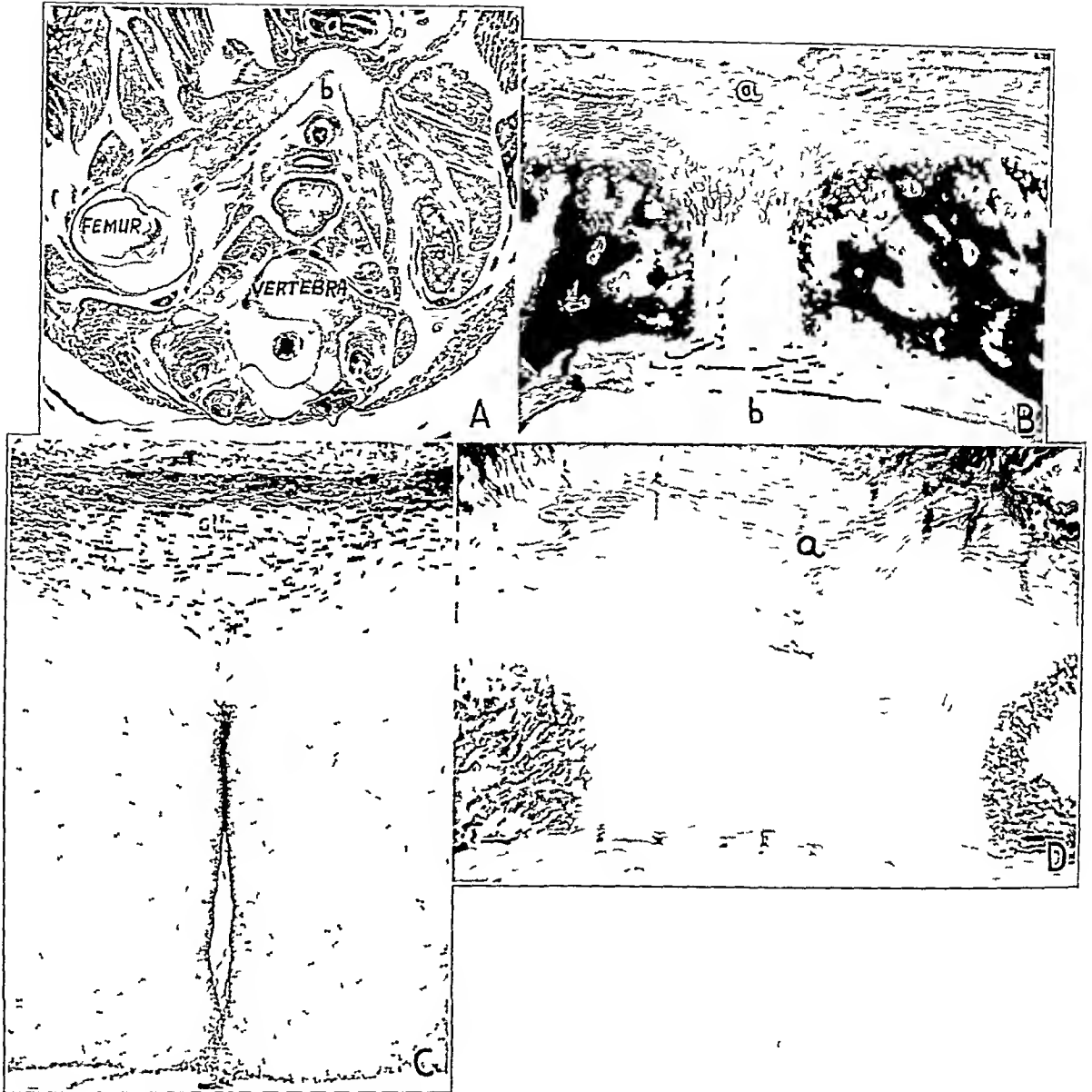


Fig 1—*A*, photomicrograph of the region of the symphysis pubis in a new-born rat, reduced from  $\times 80$ . Note the uniform plaque of hyaline cartilage which binds both pubic bones, *a* is the anterior and *b* the posterior ligament. The latter faces the peritoneal cavity. *B*, photomicrograph of a similar region in an adult rat, reduced from  $\times 80$ . Note the pubic bones and their respective growth plates. A wide layer of hyaline cartilage connects them, *a* is the anterior and *b* the posterior ligament. *C*, photomicrograph of the symphysis pubis from a human fetus at approximately 4 months, reduced from  $\times 80$ . Note the anterior ligament (*a*) and its invagination between the two embryonic cartilage plates. A cleft is present in the posterior portion of this projection. *D*, photomicrograph of the symphysis pubis from a new-born infant, reduced from  $\times 8$ . Note the anterior ligament (*a*) and its invagination between the two pubic cartilage end-plates.

In the case of the upper end of the femur and lower end of the humerus, involvement of the joint was the rule, owing to the anatomic relation of the epiphyseal line to the joint, and in these cases the epiphysis was usually destroyed.

The penalty for delayed diagnosis is the prolongation of toxemia, the multiplication of local complications, the development of secondary lesions in other bones and the destruction of the growing cells in the epiphyseal line, which causes various deformities, all of which prolong the course of the disease and increase the mortality.

TABLE 3—*The Effect of Inflammation on the Epiphysis Indicating the Location and Degree of the Arrest in Growth*

Location	Complete	Incomplete
Femur*	Lower 2 Upper 5	Lower 8 Upper 5
Tibia	Lower 0 Upper 2	Lower 4 Upper 9
Humerus	Lower 3 Upper 0	Lower 2 Upper 0
Os calcis	3	1
Ulna		Lower 3
Pelvis		3
Scapula		1
Radius		Lower 1
Total	15 (16.2%)	35 (38.8%)

\* Two bones showed longitudinal overgrowth.

#### SUMMARY

A series is reported of 73 consecutive cases of acute hematogenous osteomyelitis, affecting 105 bones, with 1 death, which occurred on the third day after admission of an 8 year old girl with the disease affecting the lower end of the left femur.

The pathologic characteristics, the symptomatology and the operative treatment are briefly discussed.

An analysis of the series is made, especially in regard to the effect of inflammation on the epiphyses, with complete or incomplete interruption of growth, which occurred in 50 bones or 55.5 per cent.

In two cases in which the condition affected the lower end of the femur there was longitudinal overgrowth of  $2\frac{1}{2}$  inches (6.3 cm.) and 1 inch (2.5 cm.), respectively.

#### ABSTRACT OF DISCUSSION

DR F. C. KIDDER, Detroit. Dr. Johnston's paper is very much to the point in that it accents the necessity of early diagnosis and conservative operation.

fibrocartilage The aforementioned fibrous invagination merged with the contiguous hyaline cartilage and contained numerous blood vessels, some of the vessels penetrating the cartilage Small irregular-shaped spaces were noted, but no genuine joint cavity was discernible On the endosteal surface, the posterior cortices were lined by numerous osteoblasts The subperiosteal surface showed Howship's lacunae and osteoclasts (fig 2 *D*)

On examination of a specimen removed from the body of an 8 year old boy, nothing remarkably different was noted A similar dentate shadow was apparent at the growth zone in the roentgenographic plate Gross examination revealed turgid interpubic fibrous and fibrocartilaginous tissues Small clefts were observed in these tissues, most marked in ventral portions of sections taken from the upper part of the specimen Microscopic examination again demonstrated the undulating appearance of the growth zone, with blood vessels in the interpubic tissues A few vascular channels extended into the contiguous hyaline cartilage plates The numerous clefts noted in the interpubic tissues could be definitely attributed to degeneration and separation of the fibrous elements

The third specimen under consideration came from the body of a boy 14 years of age Death had been caused by a miliary tuberculosis Roentgenographic study of the specimen revealed unusually dentate outlines at the growth zones (fig 3 *A*) Sections made from the specimen showed on gross examination a thin midline cleft in the posterior two thirds of the interpubic fibrous tissue (fig 3 *B*) In comparison with the two specimens described previously, relative diminution in the width of the hyaline cartilage end-plates was evident The thickness of the anterior ligament was from four to six times that of the posterior ligament (fig 3 *C*) Microscopic examination confirmed the presence of the irregular-shaped cleft in the interpubic tissues, the consequence of marked degeneration and necrosis of both interpubic fibrous tissues and hyaline cartilage (fig 3 *D*) Additional foci of degeneration likewise were present in the hyaline cartilage as well as several microscopic cysts An interesting feature of this specimen was the unusually deep extension of the thick anterior ligament into the hyaline cartilage, creating a relative increase of fibrocartilage in the symphysis pubis There was no great extent to the penetration of the thin posterior ligament into the hyaline cartilage plates The considerably greater thickness and greater compactness of the posterior cortex of the pubic bones may perhaps be explained as compensation The anterior cortex was partly composed of immature bone, its marrow spaces, for the most part, were in direct contact with the anterior ligament

# THE PUBIC BONES AND THEIR SYMPHYSIS

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The roentgenographic configurations cast by the pubic bones and their symphysis have aroused my special interest. In an effort to interpret these more fully, studies have been made on seventy-five specimens of this anatomic region,<sup>1</sup> obtained post mortem. The specimens were examined histologically and roentgenographically for the purpose of elucidating the following questions: 1. How does the symphysis pubis develop and is it a true joint? 2. What should be considered its normal appearance until puberty? 3. Are there any growth changes after adolescence? 4. What changes in this area after middle age may be deemed normal? 5. What changes occur in the symphysis pubis during pregnancy? 6. What modifications are produced in this region by the local presence of pathologic tissue?

## METHOD OF STUDY

In the course of seventy-five autopsies, the portion of the body in the region of the symphysis pubis was removed. The specimens came from persons whose ages at the time of death ranged from less than 1 year to 75 years (table). Specimens from a premature and from a newly born infant were also examined. On removal, each specimen was roentgenographed in its anterior-posterior plane, after which it was cut serially in the same plane into several thin portions. Each

From the Laboratory Division, Hospital for Joint Diseases  
\* Brown Orthopedic Research Fellow

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notched, sometimes straight and often dentate<sup>6</sup> Todd discerned ten different stages through which the pubic bone of the adult passes in its development

When specimens of the symphysis pubis removed at autopsy from adults were selected for study, such as were apparently involved by disease (except arthritis) were excluded

On gross examination it was possible to produce slight motion in several specimens removed from the bodies of adult males and nulliparas However, only when the pubic bones were forced anteriorly was motion obtained Widening the interpubic space was almost impossible

There was no uniformity in the roentgenographic appearance of the subchondral zones, in some, traces of the original undulated structure were still distinguishable (fig 5 *A*), in others, flat sclerotic zones only were seen The latter observation was made particularly in specimens

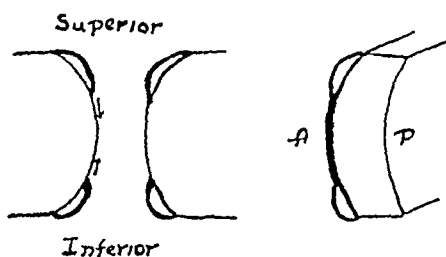


Fig 4—A schematic representation of the superior and inferior “retrogressive epiphyses” of the pubic bones They attempt to meet and fuse along the anterior surfaces *A*, anterior, *P*, posterior

taken from adults of from 40 to 50 years (fig 6) Some porosis of the subchondral zones was manifested in the greater portion of specimens taken from adults past 50 years Definite sclerotic subchondral zones persisted in several specimens taken from adults between 50 and 80 years of age (fig 7 *A*) In a number of roentgenograms of group B, the ventral rampart or anterior corner—the ledge of bone formed along the anterior surface of the pubic bone close to the symphyseal face (described)—was clearly demonstrated (fig 5 *A*)

In macroscopic examination of serial sections, the clearly visible anterior ligament showed its decussating fibers deeply injected into the

6 Krauss, F Ueber Symphysensprengung, *Zentralbl f Chir* **57** 134, 1930  
Chamberlain, W E The Symphysis Pubis in the Roentgen Examination of the Sacro-Iliac Joint, *Am J Roentgenol* **24** 621 (Dec) 1930 Sack, G M Zur Pathologie der Symphyse, *Rontgenpraxis* **5** 566 (Aug) 1933 Burman, M S, Weinkle, I N, and Langsam, M J Adolescent Osteochondritis of the Symphysis Pubis, *J Bone & Joint Surg* **16** 649 (July) 1934

bones<sup>3</sup> (fig 1 *A* and *B*) In man the fibrous tissue between the cartilaginous formations is incompletely transformed into hyaline cartilage This communicating mesenchyme is subject to conversion in some degree, into fibrous tissue or into fibrous or hyaline cartilage Very early even in intra-uterine life clefts may be seen in that interstitially placed connective tissue<sup>4</sup> This was noted in the posterior portion of the symphysis pubis of a human fetus (at 4 months fig 1 *C*) In the newly born infant, the undifferentiated mesenchyme appears as an insertion of fibrous tissue or fibrocartilage between the cartilaginous portions of the pubic bones This tissue may or may not contain the clefts mentioned It may therefore be inferred that there is no basis for considering the pubic symphysis as a true joint region (fig 1 *D*)

The results of the present studies will be presented as (*A*) appearances in the young and (*B*) appearances in the adult

#### GROUP A (AGES 1 TO 17 YEARS)

Three typical specimens will be described They illustrate clearly the characteristic roentgenographic gross and histologic observations in the young

Roentgenographic examination of a specimen removed from the body of a 3 year old child plainly demonstrated the beginning of a dentate appearance in the symphyseal ends (fig 2 *A*) This was a consistent observation in all roentgenograms of pubic bones removed from the bodies of infants

On gross examination it was found that the pubic bones in the region of the symphysis were bound together by four external ligaments (superior, inferior, anterior and posterior) The application of considerable force in the anterior direction relaxed the anterior ligament, although there was marked resistance to motion in any of the other directions On section of the various specimens in the anterior-posterior plane, the thick anterior ligament was clearly disclosed with its projection between the end-plates of the pubic bones The growth zones at the symphyseal ends of the pubic bones presented a slightly serrated surface (fig 2 *B*) The gross appearance was thus entirely in conformity with that observed on roentgenographic examination The fibrous tissue between the cartilaginous ends of the pubic bones was recognized by roentgenographic examination as a dense linear shadow (fig 2 *C*)

3 As Chapman points out the symphysis pubis may be entirely absent in rodents As a substitute, the right rectus muscle is attached to the left pubic bone and the left rectus to the right pubic bone (Chapman R N A Study of the Correlation of the Pelvic Structure and the Habits of Certain Burrowing Mammals, *Am J Anat* 25 185 [March] 1919)

4 Ruth E B The Study of the Development of the Mammalian Pelvis, *Anat Rec* 53-54 207 (July) 1932



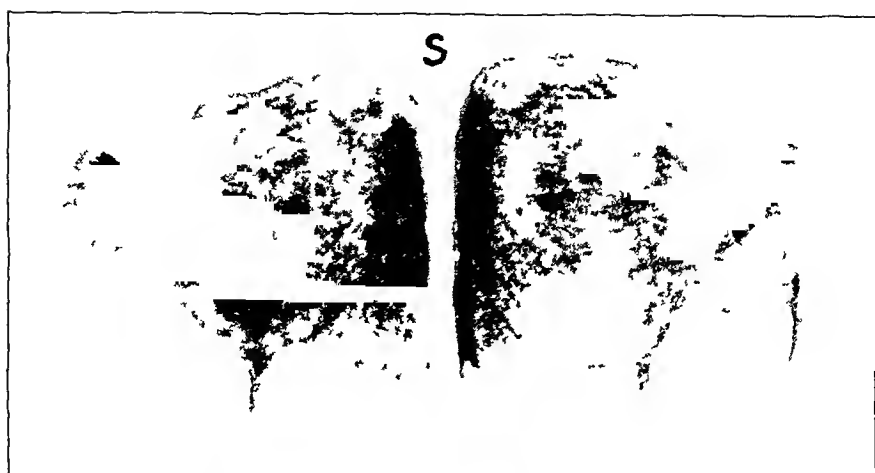


Fig 6—Roentgenogram of the pubic bones removed from a man 40 years of age, showing dense subchondral zones. Very little irregularity is noted. The superior surface of the symphysis pubis is marked *s*.

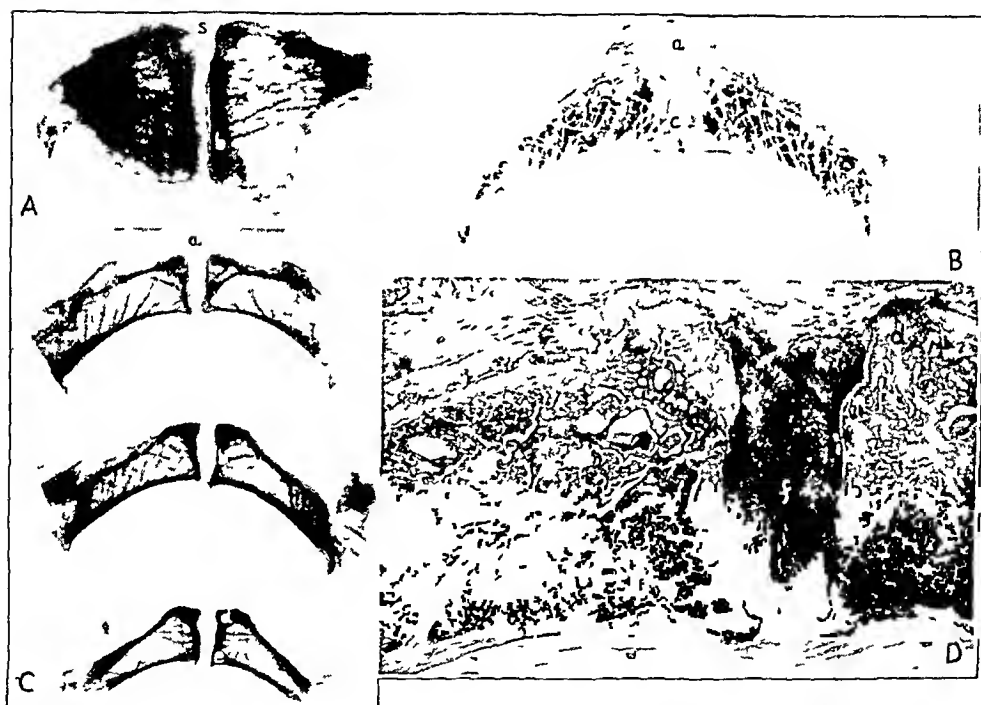


Fig 7—*A*, roentgenogram of the pubic bones removed from a man 53 years old, disclosing marked sclerosis of the subchondral regions (*b*). The superior surface is labeled *s*. *B*, photograph of a sliver cut from the specimen shown in *A* in an anteroposterior plane, exhibiting the thick anterior ligament (*a*). The fibrocartilaginous symphysis pubis contains a cleft in its posterior aspect (*c*). *C*, roentgenogram of several slivers cut from the same specimen in an anteroposterior plane, demonstrating the thick anterior ligament (*a*). The sclerotic subchondral zones (*b*), the anterior corners (*d*) and the prominent posterior corners (*e*) are clearly seen. *D*, photomicrograph of the section prepared from the middle sliver, reduced from  $\times 5$ . It reveals very thick subchondral zones (*b*) and anterior corners (*d*). The posterior corners (*e*) are prominent. Note that the interpubic tissue consists mainly of fibrocartilage (*f*). A few fissures are present in it.

On histologic examination the hyaline cartilage plates of the specimen (from the 3 year old child) were quite thick and were bound together by a layer of fibrous tissue. The latter extended about seven eighths of the anterior-posterior distance of the symphysis pubis. The remaining (posterior) one eighth was occupied by a semilunar bridge of



Fig 2—4, roentgenogram of the pubic bones from a 3 year old girl showing the beginning of a serrated appearance of the growth plates. B, photograph of two slivers sectioned from the same specimen in the anteroposterior plane, showing the wide pubic cartilages separated by a fibrous layer. Note the thin posterior ligament (b). C, roentgenogram of these two slivers, showing the projection of the anterior ligament between the two hyaline cartilage plates. D, photomicrograph of one of the slivers, reduced from X 6. Note the anterior ligament (a) and its projection (c) between the hyaline cartilage plates. The growth zones are serrated in appearance (d). The posterior ligament (b) is thin. Note the blood vessel (c) in the hyaline cartilage.

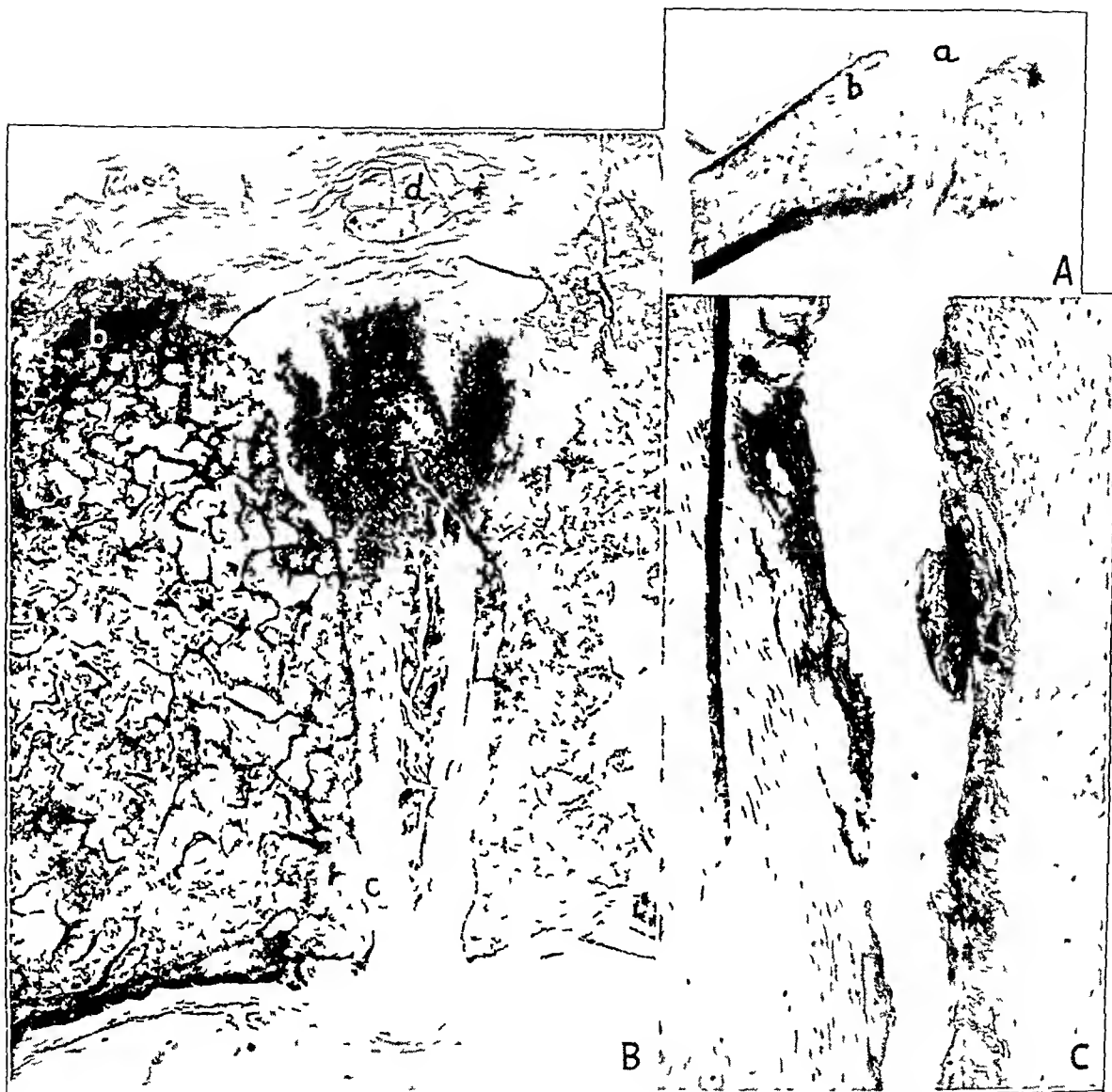


Fig 8—*A*, specimen removed from a nullipara 55 years old. The sliver was sectioned in the anteroposterior plane. The anterior portion is marked *a*. The roentgenogram demonstrates a cystic space in the anterior corner marked *b*. *B*, photomicrograph of the histologic section prepared from the sliver, reduced from  $\times 6$ . The cyst (*b*) is seen to be the result of a cartilaginous herniation. There is irregular fissuring of the symphysis pubis. A small segment of it is still of the hyaline variety (*c*). A degenerative cyst may be noted in the anterior ligament (*d*). *C*, a high power photomicrograph reveals that the cleft in the fibrosed pubic cartilage is bordered by degenerated and necrotic fibrillar cartilage. Note the island of necrotic cartilage in the fissure, reduced from  $\times 100$ .

GROUP B (ADULTS)

In the usual development of pubic bones 'retrogressive epiphyses' appear after puberty Todd<sup>5</sup> found these bony nodules (not true centers of ossification) on the superior and inferior aspects of the ventral surface of each pubic bone near the symphyseal face (fig 4) Although highly erratic in their mode of development they generally tend to meet and fuse along the ventral border of each pubic bone Changes such as

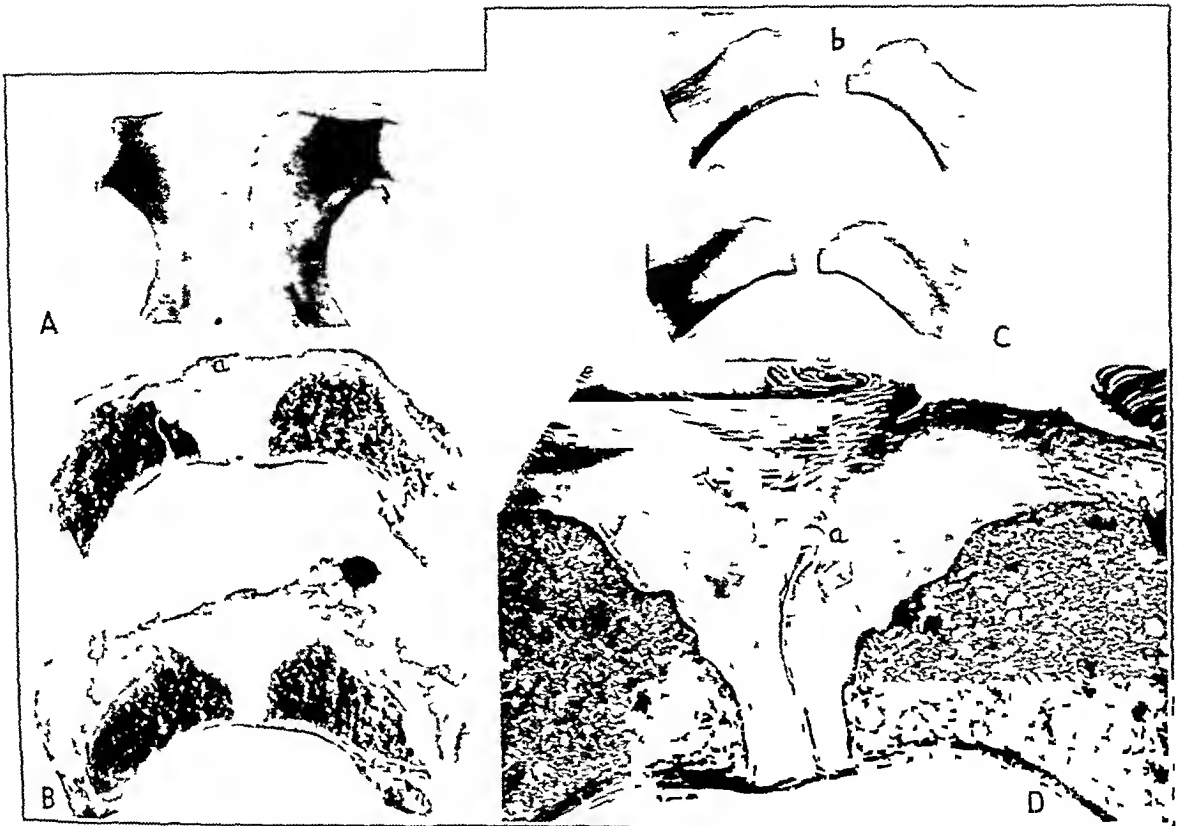


Fig 3—*A*, roentgenogram of the pubic bones removed from a 14 year old youth showing an unusual serrated outline at the growth zones *B* photograph of slivers sectioned in the anteroposterior planes from the specimen shown in 4, revealing the fibrous interpubic sheath In it is a very thin cleft The anterior ligament is marked *a* *C*, roentgenogram of these slivers disclosing the dentated configuration of the growth plates Note the greater width of the interpubic tissue in its anterior portion (*b*) *D* photomicrograph of one of the slivers reduced from  $\times 5$  It demonstrates the cleft in the interpubic tissue Note the invasion of the hyaline cartilage by the anterior ligament (*a*)

the cessation of endochondral ossification result in the formation of a subchondral bony plate Its appearance, varying widely, is sometimes

<sup>5</sup> Todd, T W Age Changes in the Pubic Bone, *Am J Phys Anthropol* 3 285 (Jul) 1920, 4 1 (Jan) 1921, 4 333 (Oct) 1921 14 255 (April) 1930

No true synovial membrane or lining was apparent at the borders of the clefts and fissures in the interpubic tissues. These cracks revealed themselves as degenerative effects, the tissue at their borders evidencing focal or generalized degeneration and necrosis (fig 8 C). Cartilage some distance from the fissures gave like evidence of mild or advanced degeneration (demonstrated by poor staining of nuclei and edema of the matrix, mucoid or fatty in nature). Groups of regenerating cartilage cells appeared in the border tissue, while islands of necrotic, living or regenerating cartilage and amorphous detritus were seen in the interpubic tissues. In specimens from male adults over 50 years of age, where no fissures were discernible, the interpubic area consisted solely of fibrocartilage, occasionally with increased amounts of mucoid that gave a semblance of hyaline cartilage.

**Subchondral Zone** Compact lamellar bone constituted the structure of the subchondral bony plates in the greater number of sections. In several, however, from adults over 50 years of age, porosis and focal necrosis existed, while in a few there were inclusions or herniations of either fibrous or hyaline cartilage. When the latter was present there was a slight appearance of endochondral ossification. The interpubic tissues were invaded by vascular channels of subchondral origin. Therefrom ensued the formation of bony osteophytes and marrow spaces in the interpubic tissues (fig 9 B). Osteophytes may similarly be situated in the provisional zone of calcification at either the anterior or the posterior corners of the pubic bones.

**Cortices** Posteriorly, the cortices were somewhat thicker than anteriorly. In some specimens taken from elderly adults, scattered areas of aseptic necrosis were occasionally noted.

**Ligaments** The decussating fibers of the ligaments were deeply inserted in the interpubic tissues. Shorter fibers attached themselves to the corners, thus firmly fixing the pubic bones. Like the interpubic tissues, the ligaments may suffer degenerative changes with the resultant occurrence of clefts and cysts (fig 8 B). The cysts may contain necrotic ligamentous tissue and occasionally islands of either dead or living cartilage.

**Specimens from Multiparas** It is recognized that pregnancy induces alterations in the appearance of the pubic bones and of the symphysis pubis. Osteoclastic resorption of the symphyseal ends of the pubic bones has been observed in pregnant guinea-pigs.<sup>7</sup> Investigators

<sup>7</sup> Todd, W. T. The Pubic Symphysis of the Guinea Pig in Relation to Pregnancy and Parturition, *Am J Anat* 31 345 (March) 1923. Kawata, S. On the Morphological Changes of the Symphysis Pubo-Ischiadica in the Guinea Pig During Pregnancy, *Folia anat japon* 2 370, 1924. Eymer, H., and Lang, F. J. Anatomische Untersuchungen der Symphyse der Frau im Hinblick auf die

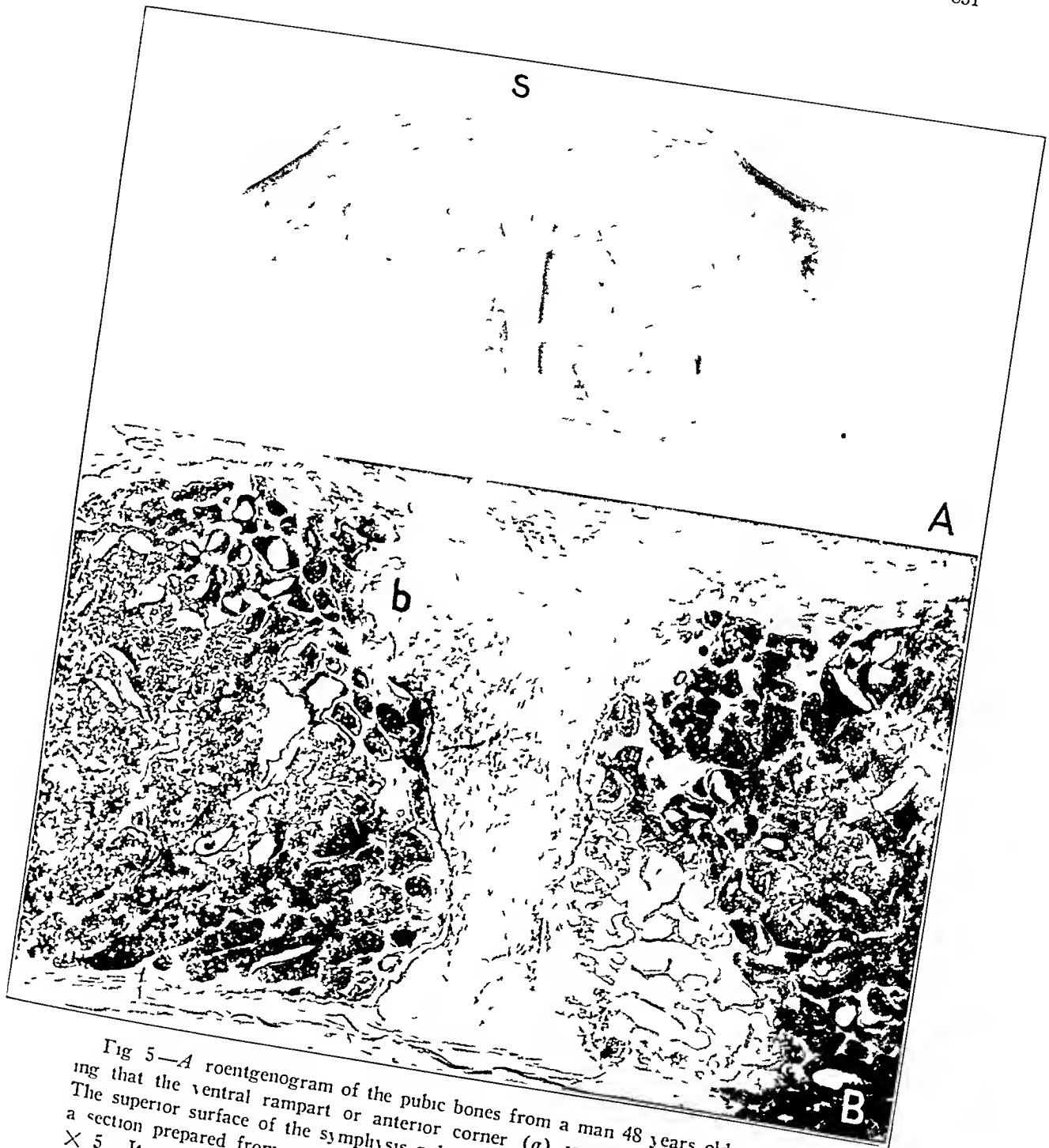


Fig 5—*A* roentgenogram of the pubic bones from a man 48 years old, revealing that the ventral rampart or anterior corner (*a*) is serrated in appearance. The superior surface of the symphysis pubis is labeled *s*. *B*, photomicrograph of a section prepared from a sliver cut in the anteroposterior plane, reduced from  $\times 5$ . It reveals no fissures in the symphysis pubis. Note the absence of the anterior corner in the left pubic bone (*b*).

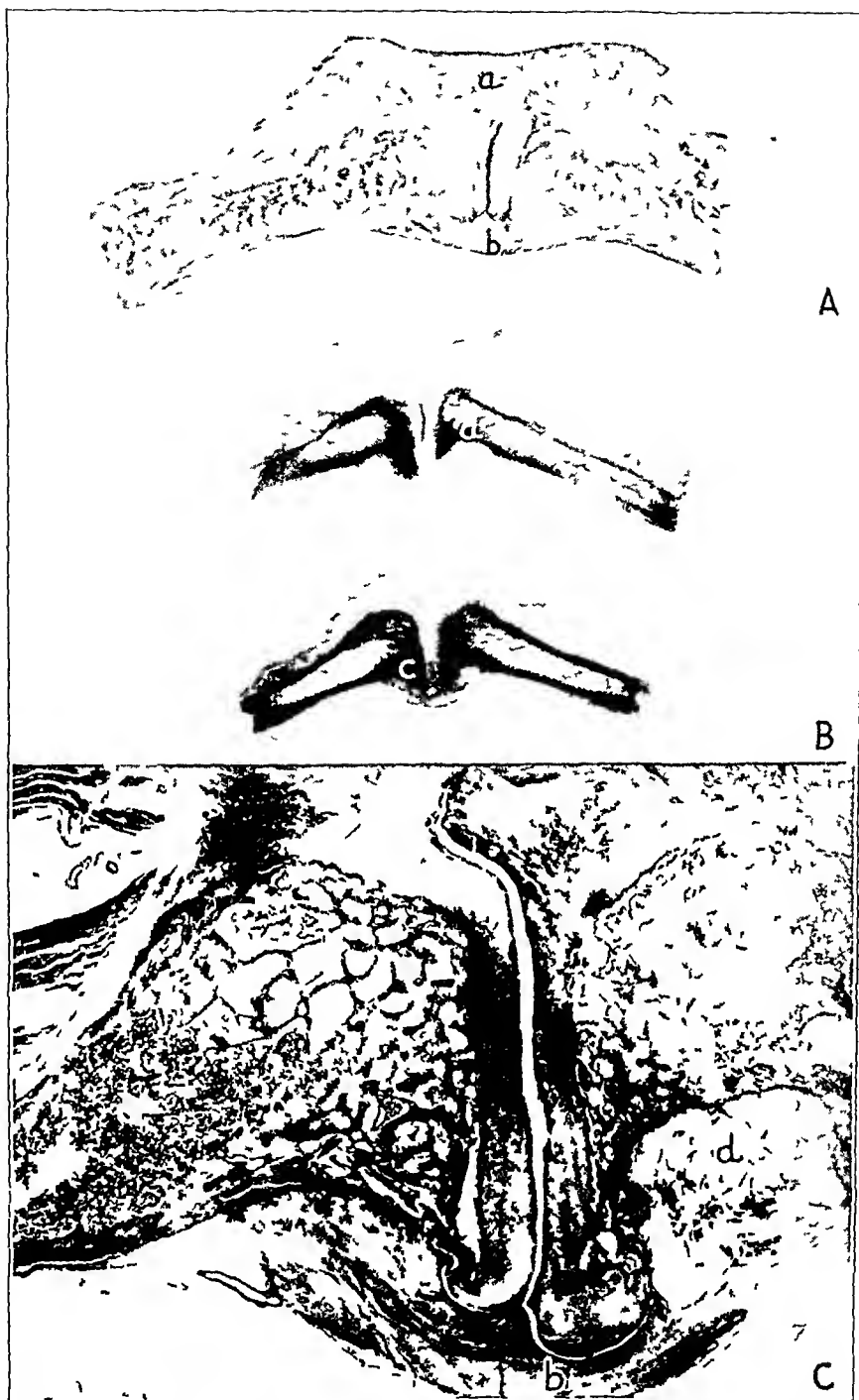


Fig 10—Photograph of a sliver from a specimen from a multipara 67 years old. It was sectioned in the anteroposterior plane. Note the thick posterior ligament (b) and the anterior ligament (a), which is continuous with the interpubic tissues and has in it a large fissure. B, roentgenogram of two slivers showing marked prominence of the posterior corners (c). Note the depressions in the posterior cortices for the insertions of the posterior ligament (d). C, photomicrograph of one of the slivers, revealing a large cleft in the symphysis pubis, reduced from  $\times 6$ . This is continuous with those in the posterior ligament (b). The niche in the posterior cortex (d) is clearly seen.

interpubic cartilage. The ligament was thicker than the posterior one (fig 7 B), except in specimens taken from multiparas.

Contrary to the appearance in the young, in whom the end-plates of the pubic bones are composed of thick zones of hyaline cartilage, only small segments of such cartilage appeared in the adult group. Those seen were in the anterior or the posterior portions of the symphysis pubis close to the pubic bones. The rest of the cartilage end-plate which had been hyaline was transformed into fibrocartilage or was extremely fibrillated. The cartilaginous end-plates varied in color from brownish yellow to distinct yellow.

In group B, again, the irregular clefts were manifest in many of the specimens. They appeared either in the middle of the interpubic tissue or close to the subchondral zones, extending from the anterior to the posterior ligament and from the superior to the inferior ligament. Some were observed only in the anterior, the middle, or even the posterior third of the symphysis pubis. Sometimes, the latter clefts were extensions of those in the anterior or the posterior ligament. Some of these clefts were wide enough to admit the bulbous head of an ordinary pin, several clefts had irregular branches.

Roentgenographic examination of serial sections demonstrated clearly the subchondral zones as well as the anterior corners arising from the "retrogressive epiphyses" (fig 7 C). In some cases, the subchondral zones of the right and left pubic bones were not parallel to each other. They diverged toward the anterior cortices. Roentgenographic examination of a few sections disclosed small cystlike shadows varying in size from 2 to 6 mm. in or near the subchondral zones (fig 8 A). Histologic studies revealed them as either cartilaginous herniations or discrete islands of cartilage (fig 8). Also present, were small osteophytes projecting from the subchondral zones into the symphysis pubis (c, fig 9 A). Bony projections were observed in some to be near or at the posterior corners, i. e., the junction of the posterior cortex and the symphyseal face.

*Histologic Studies*—Interpubic Tissue. Each section studied in group B had definite fibrillation of some parts of the hyaline cartilage, usually with marked fibrous invasion of the remaining hyaline cartilage (fig 7 D). This demonstrated its cause to be the expansion of the anterior ligament with its fibrous projection at the expense of the hyaline cartilage. Close to the subchondral bone, small remnants of hyaline cartilage remained intact. The clefts were again observed in the interpubic tissues. In specimens from males (fig 9 C) they were rather limited, and several such specimens were totally without any evidence of fissures (fig 5 B). Irregular fissuring was observed to a slightly greater extent in specimens obtained from nulliparas (fig 8 B).



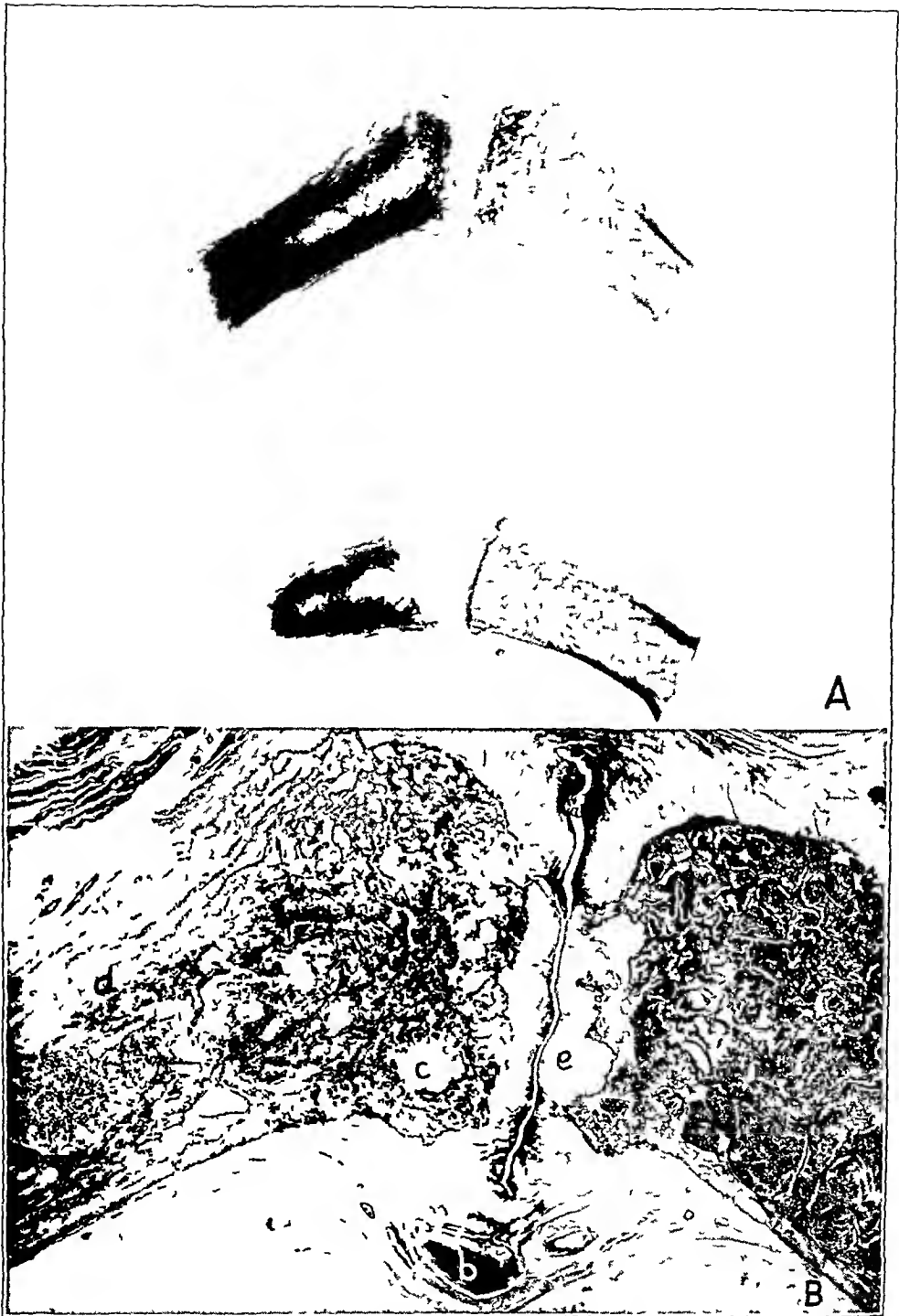


Fig 11—*A*, roentgenogram of slivers of a specimen from a multipara 53 years old. The slivers were sectioned from the specimen in an anteroposterior plane. Note the sclerosis of the right pubic bone—Paget's disease. *B*, photomicrograph of one of the slivers, reduced from  $\times 5$ . It demonstrates a cleft in the interpubic tissue (*a*), a degenerative cyst in the thickened posterior ligament (*b*), numerous cartilaginous islands in the marrow (*c*), thickened cortices and closely set bone trabeculae (*d*) and newly formed pubic cartilage (*e*).

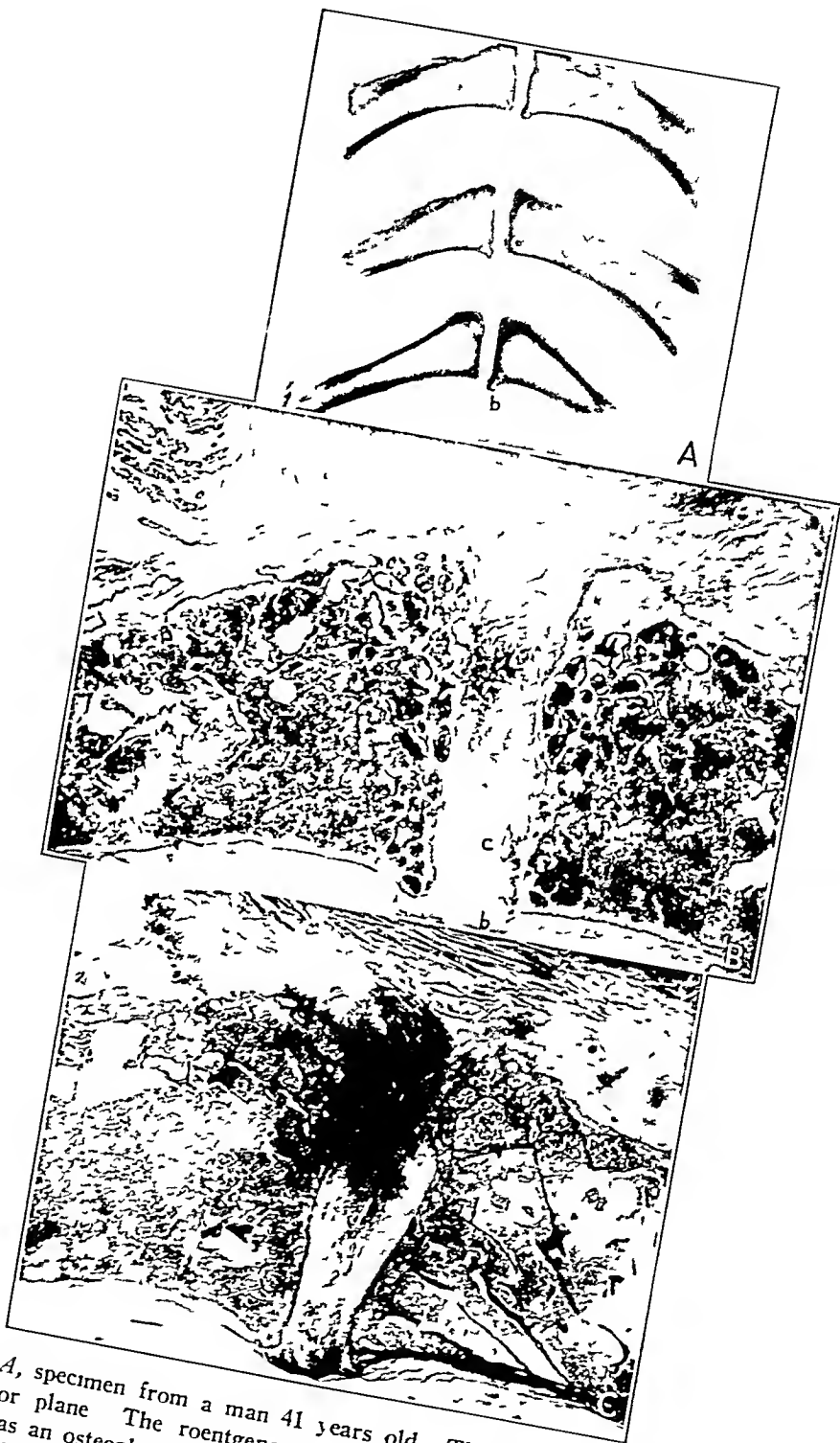


Fig 9—*A*, specimen from a man 41 years old. The slivers were cut in the anteroposterior plane. The roentgenogram reveals prominent posterior corners (*b*) as well as an osteophyte projecting into the interpubic tissue (*c*). *B*, photomicrograph of the middle sliver, reduced from  $\times 5$ . Note the osteophyte in the interpubic tissue (*c*), also that at the posterior corner (*b*). *C*, photomicrograph of a section prepared from a sliver cut in the anteroposterior plane, reduced from  $\times 5$ . The specimen is from a man 55 years old. A few fissures may be seen in the fibrocartilaginous symphysis pubis.

# SURVIVAL OF AN AUTOPLASTIC PARATHYROID TRANSPLANT IN A PATIENT WITHOUT PARATHYROID DEFICIENCY

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Autoplastic transplantation of parathyroid tissue has been practiced by a number of surgeons in connection with operations on the thyroid gland when one or more parathyroid glandules have been accidentally removed. This procedure has been advocated, particularly by Lahey, as a means of preventing the occasional occurrence of postoperative tetany. As far as we are aware, however, there has been no final proof of the survival of the transplant in these cases. Cattell<sup>1</sup> observed post-operative tetany in one of his patients in whom parathyroid tissue had been reimplanted between the fibers of the sternocleidomastoid muscle. The facts that the calcium content of the blood gradually returned to normal in the course of several weeks and that the tetany spontaneously and permanently disappeared were taken to indicate that the transplant had survived and was functionally active. There was no opportunity, however, to check this by microscopic study.

On the basis of Halsted's experimental work, it has been generally felt that these grafts will not survive unless there is a state of parathyroid deficiency following the transplantation, such as occurred in the patient observed by Cattell. We have studied the fate of parathyroid autografts in the dog under varying degrees of parathyroid deficiency and have demonstrated that, contrary to the general belief, these transplants will survive regardless of the physiologic need of the organism for parathyroid tissue.<sup>2</sup>

The clinical corroboration of this experimental finding has recently been observed.

A woman, aged 61, was subjected by us to total thyroidectomy on Feb. 4, 1933, because of intractable cardiac disease with severe angina pectoris and a previous history of coronary thrombosis. After removal the gland was carefully examined

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From the Surgical Service of the Peter Bent Brigham Hospital

1 Cattell, R. B. Parathyroid Transplantation. Report of Autografts of Parathyroid Glands Removed During Thyroidectomy, *Am J Surg* 74 (July) 1929.

2 Shambaugh, P. Autotransplantation of Parathyroid Gland in the Dog. An Evaluation of Halsted's Law of Deficiency, *Arch Surg* 32:709 (April) 1936.

heretofore have demonstrated that the adult male guinea-pig has a cartilaginous, and the adult female a fibrous, symphysis pubis. Repeated injections of theelin (or a similar product) into the castrated adult guinea-pig causes transformation of the symphysis from cartilaginous to fibrous. Additional injection of blood from a pregnant animal into the feminized guinea-pig induces relaxation of the fibrous symphysis pubis.<sup>8</sup> It has been successfully demonstrated that in the human being relaxation of the symphysis pubis occurs during pregnancy.<sup>9</sup>

Specimens taken from multiparas were easily differentiated as such. Their most obvious distinction lay in the thickness of the posterior ligament, which appeared as a massive rounded elevation on the posterior surface of the symphysis pubis (fig. 10 A). Examination of the sections

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8 Hisaw, F. L. The Corpus Luteum Hormone. Experimental Relaxation of the Pelvic Ligaments of the Guinea Pig, *Physiol Zool* **2** 59 (Jan.) 1929. Fevold, H. L., Hisaw, F. L., and Meyer, R. K. Isolation of the Relaxative Hormone of the Corpus Luteum, *Proc Soc Exper Biol & Med* **27** 604 (March) 1930. Hisaw, F. L. Physiology of the Corpus Luteum in Allen, E. Sex and Internal Secretions, Baltimore, Williams & Wilkins Company, 1932, p. 499. Pommerenke, W. T. The Cyclic Relaxation of the Pelvic Ligaments in the Guinea Pig, *Anat Rec* **57** 361 (Nov.) 1933. Tapfer, S., and Haslhofer, L. Hormonale Weiterstellung des Beckens im Tierversuch, *Arch f Gynak* **159** 313, 1935.

9 Duncan, J. M. Researches in Obstetrics, Edinburgh, A. & C. Black, Ltd., 1868. Snelling, F. G. Relaxation of the Pelvic Symphyses During Pregnancy and Parturition, *Am J Obst & Gynec* **2** 561 (Feb.) 1870. Eastman, T. B. Rupture of the Symphysis Pubis, *New York M J* **83** 130 (Jan.) 1906. Tuley, H. E. Rupture of the Symphysis Pubis in Labor, *Am J Obst & Gynec* **68** 852 (Nov.) 1913. Lynch, F. W. The Pelvic Articulations During Pregnancy, Labor and the Puerperium, *Surg, Gynec & Obst* **30** 575 (June) 1920. Wishner, J. G., and Mayer, L. Separation of the Symphysis Pubis, *ibid* **49** 380 (Sept.) 1929. Muller, W. Rontgenologische Untersuchungen uber die Symphyse Schwangerer, *Zentralbl f Gynak* (no 112) **55** 999, 1931. Heyman, J., and Lundqvist, A. The Symphysis Pubis in Pregnancy and Parturition, *Acta obst et gynec Scandinav* **12** 191, 1932. Reis, R. A., Baer, J. L., Arens, R. A., and Stewart, E. Traumatic Separation of the Symphysis Pubis During Spontaneous Labor, *Surg, Gynec & Obst* **55** 336 (Sept.) 1932. Boland, B. F. Separation of the Symphysis Pubis, *New England J Med* **208** 431 (Feb.) 1933. Brouha, L. Recherches sur la mobilisation de la symphyse pubienne chez le cobaye impubere, *Compt rend Soc de biol* **113** 406 (April) 1933. Barnes, J. M. The Symphysis Pubis in the Female, *Am J Roentgenol* **32** 333 (Sept.) 1934. Abramson, D., Roberts, S. A., and Wilson, P. D. Relaxation of the Pelvic Joints in Pregnancy, *Surg, Gynec & Obst* **58** 595 (March) 1934.

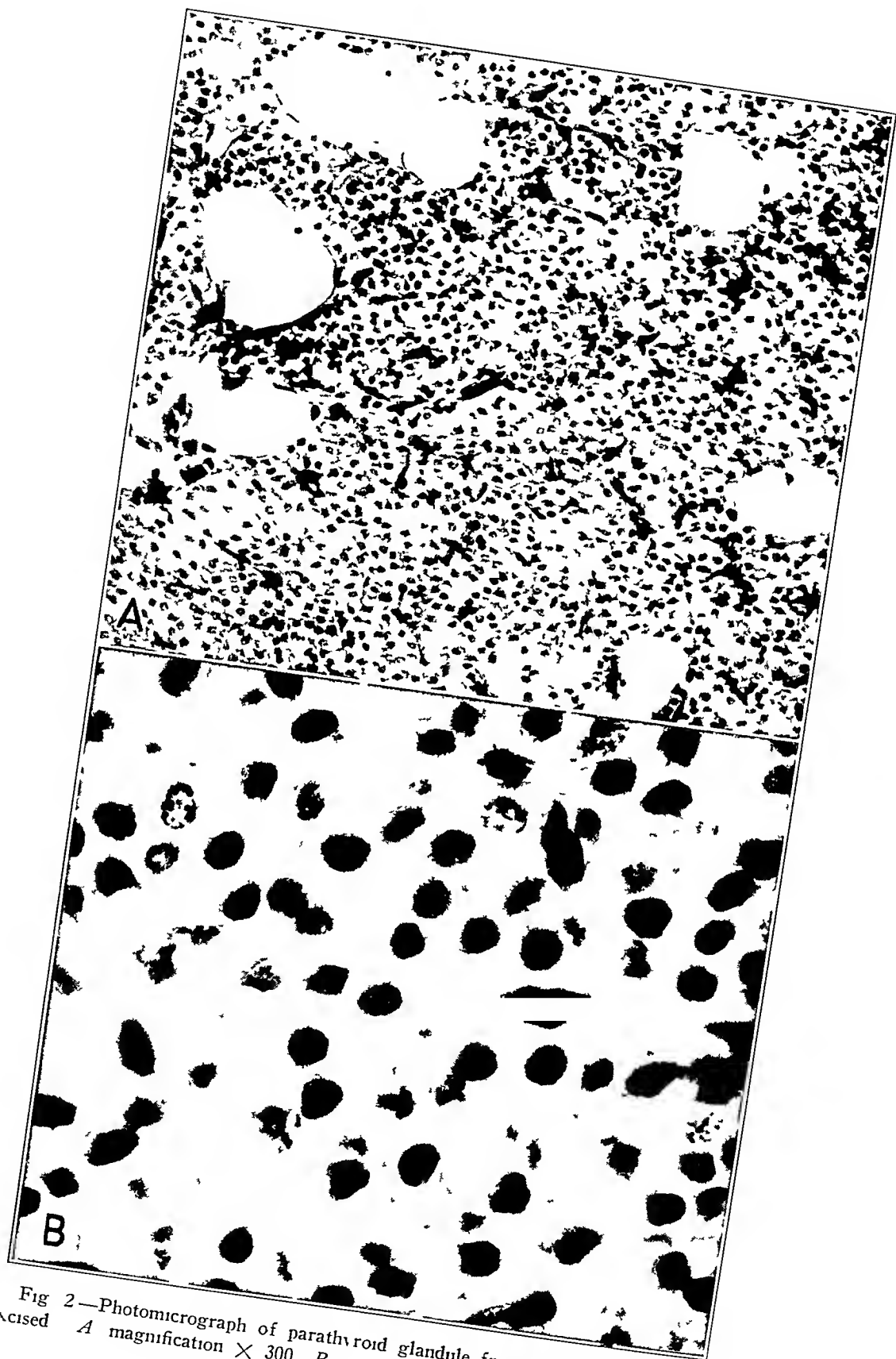


Fig 2—Photomicrograph of parathyroid glandule from which the graft was excised *A* magnification  $\times 300$ , *B*, magnification  $\times 900$

again disclosed large irregular clefts in all portions of the interpubic tissues. The cartilage plates of the pubic bones were occasionally not attached to the pubic bones and posterior ligaments. In these cases their single point of fixation was the anterior ligament. Force exerted anteriorly produced considerable motion in some of the specimens. Roentgenograms of the sections showed exaggerated posterior corners. Some specimens demonstrated symmetrical depressions on the posterior cortices near the symphyseal surfaces. Within these areas were inserted the thickened posterior ligament (fig 10 *B*). (One roentgenogram taken anteroposteriorly presented the posterior depression with a shadow like a cyst.)

Histologic examinations confirmed the gross findings. Marked degenerative changes and cleft formations had resulted in numerous cysts and channels throughout the ligaments and interpubic tissues. Many of the channels, particularly in the posterior ligament, were prolonged from one pubic bone to the other. The prominence of the thick posterior massive ligament proved to be due to the protuberance of the posterior corners in addition to an actual increase in the width of the posterior ligament with the protrusion of the posterior interpubic tissues (fig 10 *C*). (This posterior mass is reserve tissue, relaxation during pregnancy probably permits further separation of the pubic bones<sup>10</sup>.)

**Pathologic Specimens** Evidences of pathologic processes were discernible in pubic bones when no trace or far less evidence of such processes could be found elsewhere in the skeleton. In this series of examinations, Paget's disease (figs 11 *A* and *B*), idiopathic osteosclerosis, osteoporosis and metastatic foci of tumors (figs 12 *A*, *B* and *C*) were some of the conditions encountered.<sup>11</sup> Roentgenograms showed that the subchondral bone at the symphyseal face may be destroyed by pathologic tissue. Thus, in roentgenograms progressive obliteration of the shadow cast by the subchondral zone may give the clue to the presence of pathologic tissue.

#### SUMMARY AND CONCLUSIONS

Clefts in the interpubic tissues are due to degeneration, static forces may be responsible for their occurrence. Pregnancy causes relaxation and stretching of the ligaments and interpubic tissues, accentuating the

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10 The relaxation of the thickened posterior ligament may permit contact with the pelvic organs. Also, the numerous channels in the posterior ligament may provide avenues for the spread of infection, possibly constituting the basis for the occurrence of puerperal osteomyelitis in the pubic bones.

11 Histologic examination of specimens involved in Paget's disease and in nutritional osteoporosis revealed vascularization and new cartilage formation in the interpubic tissue (fig 12 *D*).

# ARTHROSCOPIC EXAMINATION OF THE KNEE JOINT

REPORT OF CASES OBSERVED IN THE COURSE OF ARTHROSCOPIC  
EXAMINATION, INCLUDING INSTANCES OF SARCOID AND  
MULTIPLE POLYPOID FIBROMATOSIS

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We have been fortunate enough in the arthroscopic examination of eighty knee joints to observe a fair number of cases remarkable enough to merit individual report. One case of xanthoma of the knee was reported separately by Kling and Sashin.<sup>1</sup>

Arthroscopy has proved of great value in this group not only in ruling out other suspected disease processes but also in providing direct visual evidence of the existing disease, unusual as it may be. Visualization was usually good, and the pathologic picture was well demonstrated. While a proper diagnosis may not be made on the basis of visual evidence, enough is seen to indicate the proper therapeutic procedure. The ultimate diagnosis has sometimes rested on the microscopic observations. This group of cases supports an oft repeated statement that diseases of the knee joint can be as difficult and complex of diagnosis as any disease process within the chest or abdomen, despite the limited means of reaction of a joint.

## SARCOID OF THE TENDON SHEATH AND JOINT

CASE 1<sup>2</sup>—A girl, aged 8 years, has been under observation for more than two years. She was first admitted to the Hospital for Joint Diseases on Sept. 19, 1932, because of swelling of the knees, ankles, elbows and wrists. The disease process was of three years' duration, first beginning in the left knee and later involving the left ankle, left foot, right knee and right ankle, in this order. The elbows and wrists were involved last, about two years before admission. The patient felt weak, and her general health was only fair, yet she was able to be up and about throughout the development of the disease. In the few weeks before

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From the Hospital for Joint Diseases, the service of Dr. Leo Mayer.

1 Kling, D. H., and Sashin, D. Hemorrhagic Villous Synovitis of the Knee Joint Due to Xanthoma, *Arch. Surg.* **30**: 52 (Jan.) 1935.

2 An abstract of this case was included in an article by Burman, M. S., Finkelstein, H., and Mayer, L. Arthroscopy of the Knee Joint, *J. Bone & Joint Surg.* **16**: 255, 1934.

degenerative processes In all specimens taken from adults, progressive (normal) degenerative manifestations could be observed

Roentgenograms of the pubic bones taken from the young demonstrated the serrated appearance of the symphyseal face as normal After puberty, growth may cause unusual conformation of the pubic face Certain rare roentgenographic appearances may be noted owing to the presence of either cartilaginous herniations or inclusions

The frequent demonstration of pathologic processes in the series studied emphasizes the importance of clinical and roentgenographic examination of the pubic region especially on the slightest suspicion of

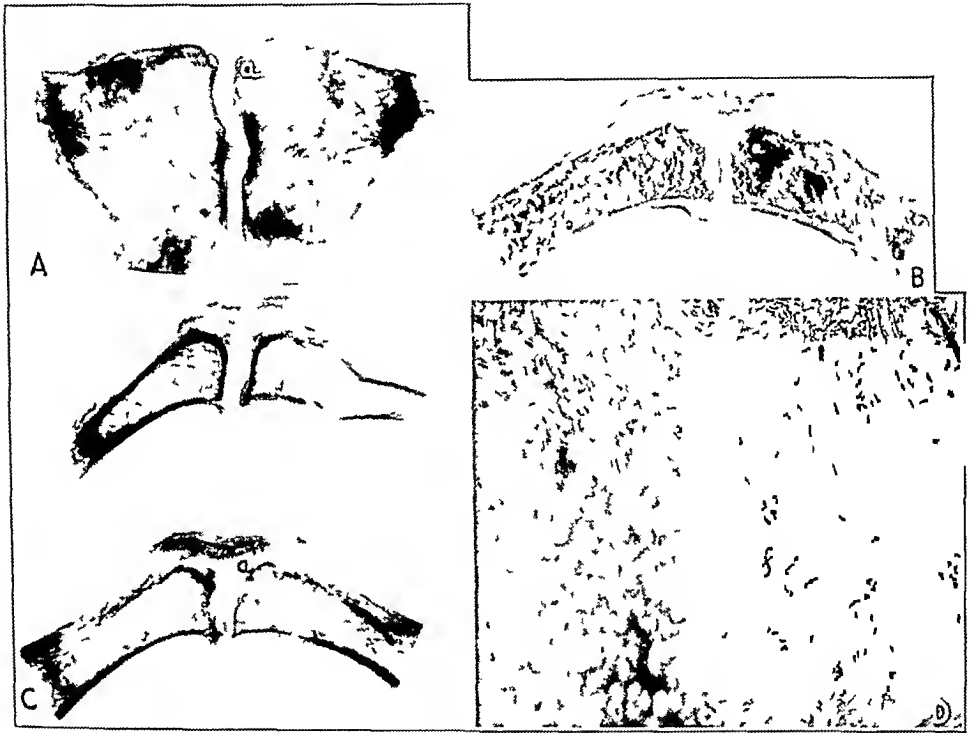


Fig 12—*A*, roentgenogram of a specimen from a nullipara 35 years old, who died from carcinoma of the stomach Observe the punched-out areas in both pubic bones A loss of the subchondral sclerosis is also apparent (*a*) *B*, photograph of a sliver sectioned from the specimen in an anteroposterior plane, which demonstrates invasion of the marrow, cortices and subchondral bone by a tumor (*a*) *C*, roentgenogram of two slivers revealing destruction of the cortices and trabeculae Note the loss of the subchondral sclerosis (*a*) *D*, photomicrograph of a specimen from a man 39 years old, reduced from  $\times 85$  There was present marked nutritional osteoporosis The photomicrograph shows a fibrous and vascular invasion of the pubic hyaline cartilage commencing from the subchondral region

an osseous lesion When postmortem examinations are limited in extent, extraction of the pubic bones for study is strongly advised, local and general osseous pathologic changes may thereby be elucidated



of the soft tissue was present on the inner aspect of both elbows. A roentgenogram made immediately after an injection of air into one of these masses showed it to be an extension of the synovial lining of the elbow and not a para-articular mass. Motion in the elbows was complete, and no heat was present about the joint. The masses on both wrists represented thickening of the tendon sheaths. There was a boggy and diffuse involvement of the common extensor tendons of the fingers, which formed a small mass on the dorsum of the hand. The



Fig. 2 (case 1)—A roentgenogram showing the cavitation in the olecranon process of the left elbow

palmar surface of the hands was not involved. There was a slight but not significant restriction in the motions of the wrist. The fingers were considered to be normal. The ankles showed boggy swelling of the peroneal tendons laterally and involvement of the extensor sheath and the sheath of the tibialis posterior muscle. The sheath of the tibialis anterior muscle was not affected on either side. Slight limitation of ankle motion was present. The masses were not hot or red.

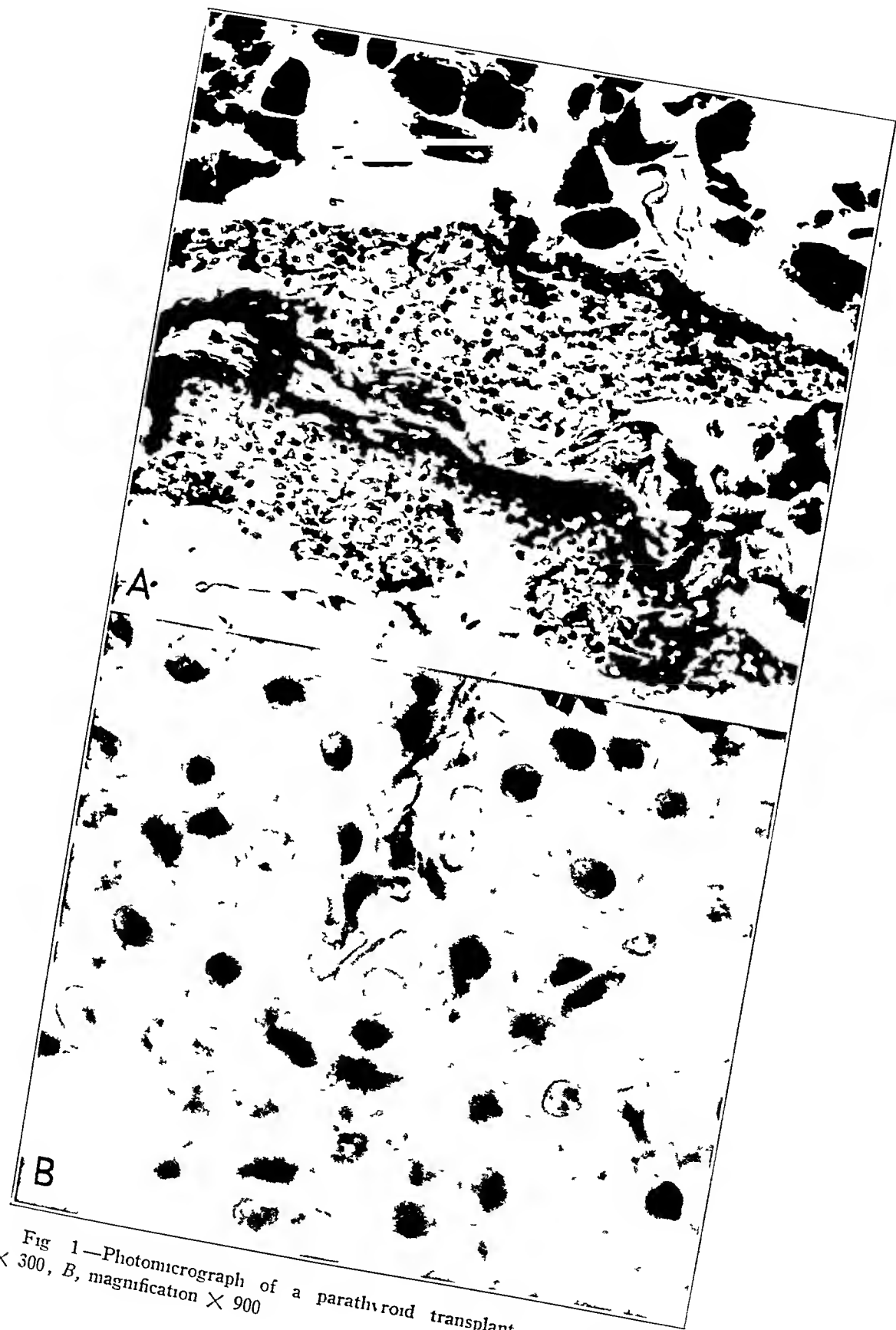


Fig 1—Photomicrograph of a parathyroid transplant *A*, magnification  $\times 300$ , *B*, magnification  $\times 900$

dilution as low as 1:100 as well as with the dilutions used as a routine. The blood picture showed no significant deviation from the normal. The red blood cell count varied from 4,160,000 to 5,440,000 and the white blood cell count from



Fig. 4 (case 1) —An arthroscopic view of the interior of the right knee joint. Observe the clusters of sarcoid tissue hanging in the joint. The fat pads are also shown.



Fig. 5 (case 1) —A section of synovia from the right wrist, showing the formation of tubercles in the synovial and subsynovial layers.

6,100 to 10,000, with a percentage of neutrophils of about 65 and a lymphocyte range of from 22 to 47 per cent. Repeated examination of specimens of synovial fluid revealed a sterile fluid, with a varying admixture of red cells. Routine and

for parathyroid tissue, and one rather large glandule, measuring 5 by 8 mm, was found on the posterior surface of the right lobe near the lower pole. A small slice of this glandule was placed between the fibers of the left sternocleidomastoid muscle, the location was marked with a silk suture, and the remainder of the glandule was saved for microscopic identification. The patient made an uneventful recovery. Further examination of the thyroid gland showed a tiny piece of parathyroid tissue, 1.5 by 0.5 mm, on the posterior aspect of the right lobe near the upper pole. The left lobe showed no trace of parathyroid tissue.

The cardiac status of the patient was improved by the operation. She was completely relieved of anginal pain for five months, when a second attack of coronary thrombosis occurred. Following this there were infrequent and relatively mild anginal seizures, until death occurred with the third attack of coronary thrombosis on Sept. 18, 1935, two years and seven months after thyroidectomy.

Careful postmortem examination of the cervical region showed no thyroid tissue remaining, and there was no parathyroid tissue on the right side. On the left side the two parathyroid glandules were identified lying in their normal position. The muscle containing the transplant was excised, and on section the graft was recovered. There was virtually no fibrosis, and the cellular structure, when compared to the original glandule from which the graft had been taken, showed no alteration (figs. 1 and 2).

It can be assumed that the anatomic deficiency in parathyroid tissue at the time the graft was placed was 50 per cent. As far as can be determined, however, there was no physiologic deficiency. The patient showed no evidence of tetany at any time, and the calcium content of the blood did not fall postoperatively. In fact, there was a slight rise from the preoperative level of 11.2 mg. per hundred cubic centimeters to 11.5 mg. ten days after operation and 11.8 mg. fourteen days after operation. A final determination seven weeks after operation showed the calcium content to be 10 mg.

A coincidental finding was that the patient had Paget's disease of the bone involving the right ilium and, to a slight extent, the skull. We believe that this probably does not signify a parathyroid deficiency and therefore does not alter the conclusion that the parathyroid autograft survived in the absence of an urgent specific physiologic demand.

ination included peculiar grapelike clusters of reddish bodies attached to the synovia. The synovia was hypertrophic, and the cartilage of the joint was normal. A biopsy specimen was removed through a punch, and microscopic examination revealed nonspecific chronic synovitis, the specimen had evidently not been taken from one of the clusters. It was determined that an unusual form of synovitis existed, one which we had never before encountered. The patient's convalescence from these multiple procedures was uneventful.

On December 9 the left peroneal sheath was explored. The sheath was filled with a reddish clump of tissue similar to that seen in the knee joint through the arthroscope. The peroneal tendon was intact, but in its course through the masses of diseased tissue it was covered with a thin pannus. Microscopic examination of the excised synovia revealed numerous cellular tubercles, with giant cells, the nuclei of which sometimes numbered 15, numerous fibroblasts and numerous epithelioid cells. These tubercles were not caseous or necrotic and were clearly demarcated from the surrounding fat. No perivascular inflammation of note was seen. Dr. Henry Jaffe, pathologist of the Hospital for Joint Diseases, considered the disease to be sarcoid, a form of tuberculous involvement most frequently encountered in the skin as Boeck's sarcoid.

The unity of the disease process in the various tendon sheaths and joints was demonstrated repeatedly on microscopic examination of tissues removed at operation. The right knee was operated on on December 28, and the red, spongelike synovia was excised. The menisci were also removed. A small pannus of this abnormal tissue was present over one condyle of the femur, and this was removed with some difficulty. Convalescence was uneventful, and motion in the knee soon became complete. The left knee was opened on Feb. 8, 1933, and on incision of the synovia the red-purple masses popped out through the line of incision. A synovectomy was done. Unfortunately an infection of a hematoma in the quadriceps bursa developed, which was relieved by proper drainage. This, however, left the knee with a partial permanent limitation of motion, extension being full but flexion being permitted only to an angle of about 150 degrees. The masses in the right peroneal sheath were removed on April 26. After these procedures the patient was discharged.

She was admitted to the hospital again in the latter part of 1933, for further surgical work. On November 29 a partial posterior synovectomy of both elbow joints was done, with removal of the masses on the inner aspects of both elbows. These communicated definitely with the elbow joint proper. At the same time the masses within the tendon sheaths of the extensor carpi radialis brevis, the extensor carpi radialis longus and the extensor digitorum longus muscles were excised. Convalescence was uneventful, and on December 13 the last operation was done, at which time the masses of diseased sarcoid tissue were removed from the extensor digitorum longus and the peroneus tertius tendon and from the sheaths of the tibialis posterior and flexor digitorum longus muscles of the right foot. The sarcoid tissue was light pink and more fatty than in the other areas operated on. In the sheath of the extensor tendons one rice body was found, this was the only rice body noted at any of the operations.

The child was soon discharged and has since been seen periodically in the clinic. On her last examination, on April 30, 1935, there was moderate effusion within the right knee, with a partial recurrence of synovial thickening. The left knee showed no change. Slight recurrence was noted along the right peroneal sheath in its lower part. A new focus had developed along the sheath of the tendon of the left tibialis anterior muscle. Another focus had developed in the tendon

admission she had noted a definite increase in the swelling of the knees, which had become painful. There had been occasional attacks of vomiting in the morning recently. There was no history of an important disease. The patient had had measles.

The child was definitely undersized and anemic and looked older than her age. She showed pronounced dental caries. Her heart and lungs were clinically normal. There was no splenomegaly or hepatomegaly. A few small shotty inguinal glands were felt, but otherwise no adenopathy was noted. The tonsils and adenoids were hypertrophied. Orthopedic examination revealed the hip joints



Fig 1 (case 1)—A photograph of the patient at the time of admission in September 1932. Note the swelling of both knee joints and the thickening of the tendon sheaths about the ankles.

and shoulder joints to be free from the disease process which involved the other large joints. Both knees were swollen, owing both to the presence of effusion within the knee and to the definite thickening of the synovial lining. The measurements of the knees were as follows: right knee,  $10\frac{3}{4}$ , 11 and  $8\frac{7}{8}$  inches (27, 28 and 22 cm), and left knee, 12, 12 and  $9\frac{1}{2}$  inches (30, 30 and 24 cm), the measurements being taken at corresponding points in the suprapatellar region, over the patella and below the patella, respectively. Extension was full, but flexion was limited to 90 degrees. No heat or local spasm was present. Swelling

Gowen,<sup>7</sup> Doub and Menagh,<sup>8</sup> Kirklin and Morton<sup>9</sup> and Sanes and Smith<sup>10</sup>

There is a general opinion that sarcoid is due to the tubercle bacillus, despite the universal absence of a positive reaction to tuberculin, despite the inability to demonstrate the tubercle bacillus and despite the negative reactions in guinea-pigs. The organism is of low virulence, and the negative reaction to tuberculin is explained by the presence of a true anergy, a state of true immunity to the bacillus. The tubercle bacillus has been demonstrated occasionally in sarcoid lesions, especially in the early stages, before the true sarcoid appearance has developed. Kyrle<sup>11</sup> called sarcoid a foreign body reaction to the bacillus of tuberculosis and its disintegration products. Microscopically, the changes are not incompatible with those observed in tuberculosis, and in our case a study of each tubercle would have invariably led to a diagnosis of tuberculosis. Others believe in a more varied etiology, and the organism of syphilis especially has been held to be a causative factor. The pros and cons of this matter were well brought out by Goeckerman.

#### SYNOVITIS OF THE KNEE JOINT CHARACTERIZED BY BODIES RESEMBLING HASSALL CORPUSCLES IN THE SYNOVIA

CASE 2—A woman, aged 37, twisted her right ankle and knee a year before she was admitted to the hospital. The right knee became painful and swollen. Aspiration was performed on the knee, and diathermy treatments were given. Subsidence of the pain took place in about a month, although a small amount of swelling remained. Nine months later severe pain and swelling of the knee again occurred, so that the patient was unable to bear weight on the right extremity. Six weeks before she was admitted to the hospital the knee again caused her to be incapacitated, so that further treatment was necessary. She walked with a knee limp on the right side, the knee being held at an angle of 170 degrees. Extension of the knee was possible to an angle of 170 degrees, and flexion only to an angle of 40 degrees. No abnormal movements were noted. Definite thickening of the synovial lining, especially in the quadriceps bursa, and enlargement of the fat pads were present. Slight tenderness existed along the line of the internal meniscus.

The roentgenogram of the knee showed no abnormalities. The only pertinent laboratory observation was a white blood cell count of 20,900. A diagnosis of

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7 Van Alstine, G. S., and Gowen, G. H. *Osteitis Tuberculosa Cystica Multiplex (Jungling)*. Report of a Case Involving the Large Long Bones with Complete Proof of Its Tuberculous Etiology, A Review of the Literature, *J. Bone & Joint Surg.* **15** 193, 1933.

8 Doub, H. P., and Menagh, F. R. *Bone Lesions in Sarcoid*, A Roentgen and Clinical Entity, *Am. J. Roentgenol.* **21** 149, 1929.

9 Kirklin, R. R., and Morton, S. A. *Roentgenologic Changes in Sarcoid and Related Lesions*, *Radiology* **16** 328, 1931.

10 Sanes, S., and Smith, W. S. *Osteitis Tuberculosa Multiplex Cystica of Fibula and Tibia*, *J. A. M. A.* **102** 1206 (April 14) 1934.

11 Kyrle, quoted by Goeckerman.<sup>5</sup>

The diagnosis was uncertain. A pediatrician who was consulted diagnosed the condition as periarticular, symmetrical disease of infectious origin, possibly associated with the dental caries. Still's disease, which was considered, was ruled out by the absence of splenomegaly, the absence of adenopathy, the absence of irregular bouts of fever in the history (and indeed during the patient's stay in the hospital there was no significant variation in the temperature) and the significant freedom of motion in the swollen joints. The association of boggy masses

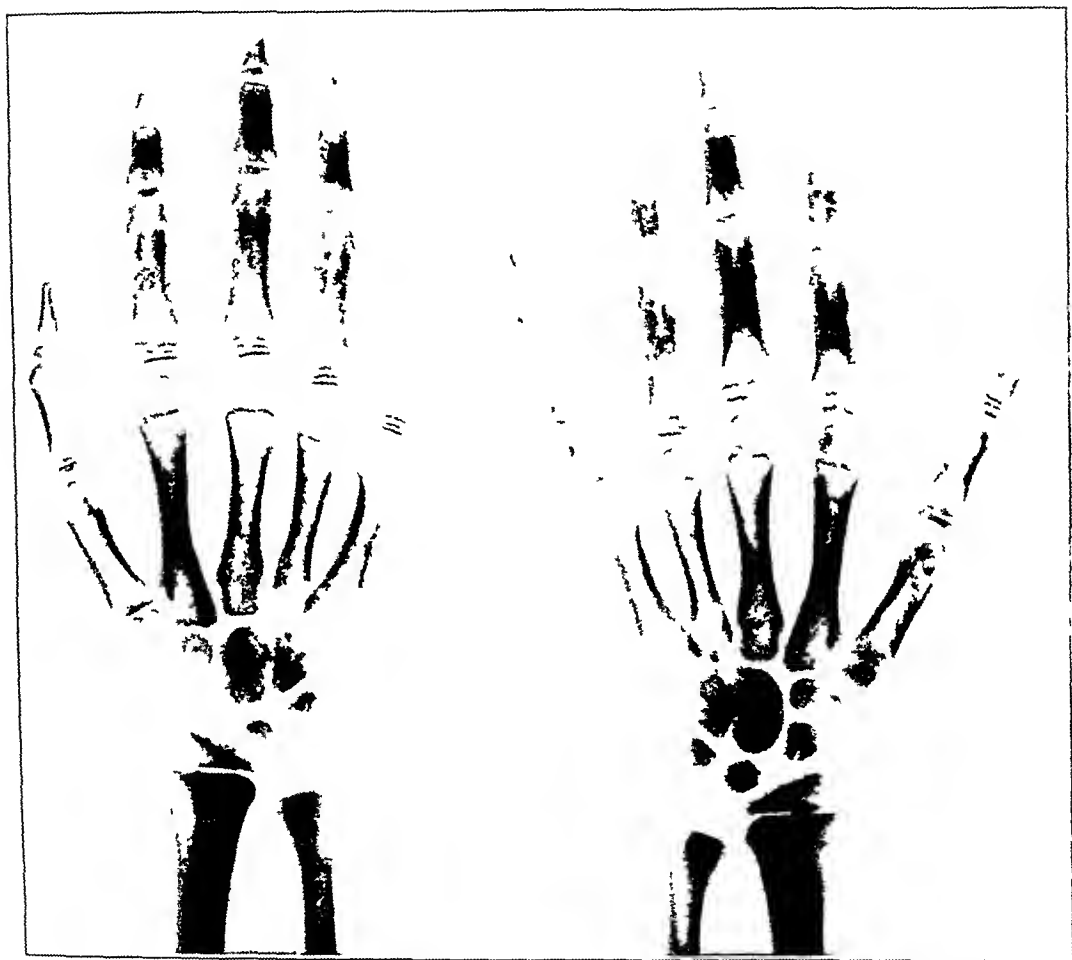


Fig 3 (case 1) —A roentgenogram showing the trabeculated arrangement of the spongiosa of the phalanges, characteristic of early sarcoid of bone. This was first pointed out by Tüngling.

with Still's disease was considered unusual. It was felt that if Still's disease were present the long duration of the illness should have brought out some of these signs.

The presence of so-called Clutton joints was suggested although the Wassermann reaction of the patient's blood on three occasions and that of her mother gave negative results.

The results of the routine laboratory procedures offered no clue as to the nature of the disease process. The reaction to tuberculin was negative with a



which at times formed little lymphoid nests. The peculiar and special character of the lesion lay in the presence of great numbers of small bodies just below the surface lining of the synovia, which at times resembled Hassall corpuscles. The bodies possessed a central core of fibrillar, acellular material, with a peripheral, concentric mass of epithelioid cells and a more concentric proliferation of other surrounding tissue cells. Some of the bodies were surrounded by lymphocytic collections, and others were not. In some regions a healing process was taking place by fibrous, cellular proliferation of these bodies. Dr Jaffe stated that such a histologic picture had not been previously observed in the laboratory.

The patient was admitted for the third time on Feb. 12, 1934, because of pain and a tired feeling in the knee on which the operation had been performed. Until recently she had been free from symptoms following the synovectomy. She also had pain in her right shoulder. Examination revealed some periarticular thickening of the knee. The patella was not as movable as it should have been. Some diffuse pain and tenderness were noted. Flexion of the knee was restricted to an angle of 90 degrees.

Arthroscopic visualization was therefore done again to determine what had happened to the joint after the synovectomy. The visualization of the joint was very good, and a mild reformation of the synovia, expressed in an irregular formation of villi most marked in the quadriceps pouch, was noted. The internal meniscus was not present, and regeneration had not taken place. Eosin introduced into the joint resulted in slight staining of the cartilage and uniform staining of the synovia. No indication for surgical intervention was seen. The patient received typhoid vaccine therapy for a short time. She was last seen in April 1935, still complaining of ache and weakness in the knee and of pain in her feet and shoulders. She is being treated as an arthritic patient.

#### MULTIPLE POLYPOID FIBROMATOSIS OF THE SYNOVIA OF THE KNEE JOINT

Multiple polypoid fibromatosis is an unusual involvement of the synovia of the knee joint, which clinically resembles nonspecific synovitis of the knee, with recurrent effusion. There is some resemblance to tuberculosis, and that condition has to be considered in the differential diagnosis. It is a true tumor of the knee, and case 3 was the first one of this type that we have encountered clinically. Dr Jacobson told us that several specimens of synovia exhibiting such a tumorous change have passed through the laboratory.

CASE 3—The patient was a Negress, aged 31, who was first seen in the dispensary in 1931. At that time she presented an effusion within the left knee joint, which had developed without trauma. The fluid was aspirated, and all efforts to prove the joint to be tuberculous were without avail. The patient did not return, nor did she seek medical attention elsewhere. The swelling of the knee had never completely subsided, and it was definitely worse during the menstrual periods. Pain had been present, especially on weight bearing. There was no history of locking. A week before her second visit to the clinic the swelling of the knee became much worse. Dull ache was associated with it.

The left knee showed marked effusion. The synovia was markedly thickened and could be felt almost as a distinct layer. Small discrete masses could be felt, which were attached to the synovia, especially one the size of a small almond.

special (Corper's method) cultures of the fluid did not yield the tubercle bacillus or, for that matter, any other organism. An intensive attempt was made to demonstrate the tubercle bacillus after the microscopic demonstration of the disease, yet repeated inoculations of guinea-pigs and intraperitoneal and intratesticular injections into rabbits did not reveal the presence of the tubercle bacillus. The tracheobronchial glands, which were said by Frazier and Hu<sup>3</sup> to be the surest site for demonstration of the tubercle bacillus in animals inoculated with material from lesions of sarcoid, were not examined in these animals.

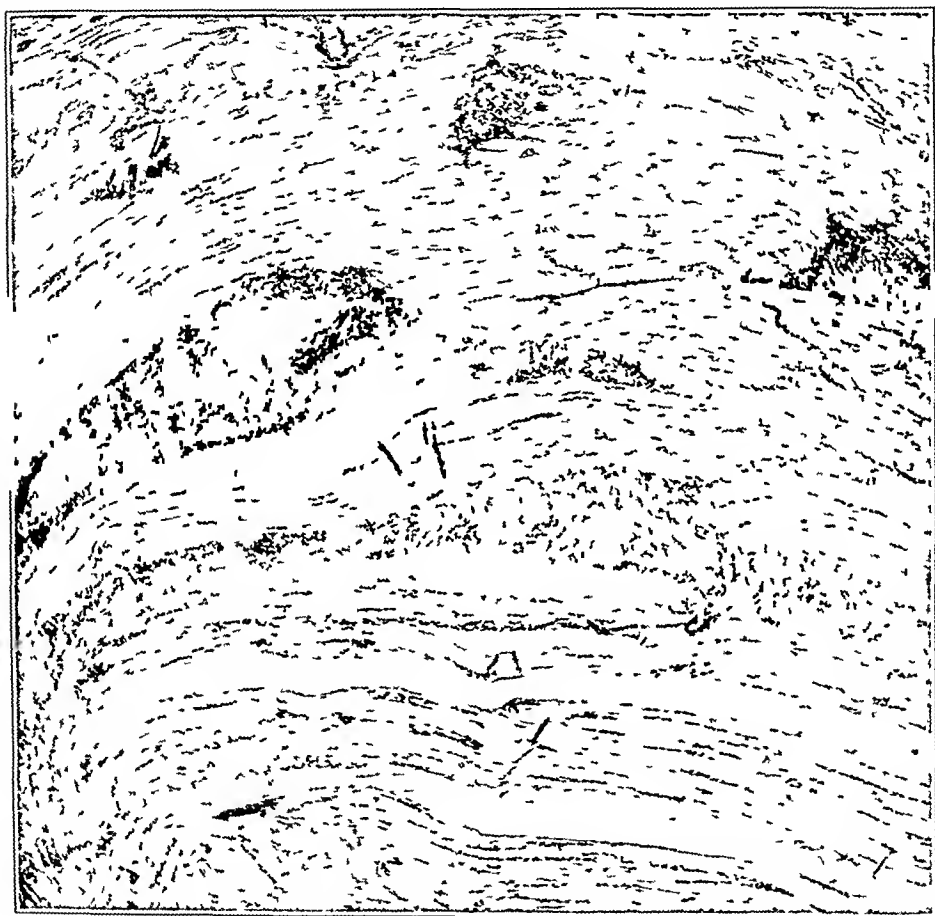


Fig 6 (case 1)—A section of tissue removed from the right elbow, showing the tubercles penetrating between the muscle bundles

On September 23 a tonsillectomy was done. On October 5 the removal of several teeth, the exploration of a small cavity in the olecranon process of the left elbow, which was demonstrable by roentgenogram, and an arthroscopic visualization of the right knee were carried out simultaneously with the patient under general anesthesia. The cavity in the olecranon process contained some granulation tissue, which yielded negative results on examination for a tuberculous process or for any specific disease. The significant observations on arthroscopic exam-

3 Frazier, C. N., and Hu, C. K. Isolation of *Treponema Pallidum* from a Subcutaneous Sarcoid. *Proc Soc Exper Biol & Med* 30: 898, 1933.

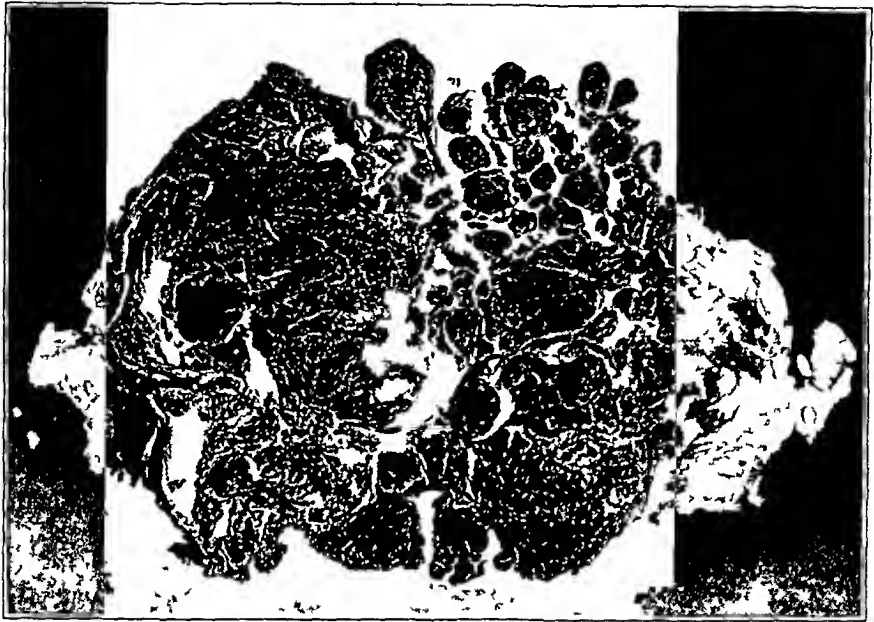


Fig 8 (case 3) —A photograph of excised synovial membrane and fat pads. Note especially the numerous pedunculated, polyp-like masses attached to the hypertrophic synovia.



Fig 9 (case 3) —A section of synovial membrane, showing villous hypertrophy, as well as a large, pedunculated nodule.

sheath on the dorsum of the left wrist. A recurrence was observed on the inner side of the left elbow. This proves that recurrence may take place despite the surgical removal of foci, although it has been established that the end-result of surgical intervention is good, since recurrence was not noted at most of the operative sites. That the disease is still active is manifested by the new foci.

The roentgenogram of all the joints showed no abnormalities save for the tiny cavitation in the ulna. This has increased slightly in size since the operation on the olecranon. On Nov 21, 1933, the left femur showed a small gouged-out area on the anterior aspect of the internal condyle. The fingers and the toes from the time of the first admission showed a peculiar punctate atrophy the significance of which was not known. In the light of the later diagnosis of sarcoid the changes in the fingers and toes are typical of the early stage of sarcoid of the bone. A note on April 7, 1933, pointed out the conical shape of the fingers, the thickening being confined mainly to the soft tissues about the shafts of the distal two phalanges. The cavitation in the olecranon process and the subsequent cavitation in the internal condyle of the femur were evidences of sarcoid of the bone.

The microscopic observations point to the unity of the disease process in this patient. Most of the tubercles were located in the subsynovial layers and in the elbows, they invaded the triceps musculature, so that tubercles were seen between muscle bundles. The synovial villi at times showed the presence of these tubercles. The invasion of the muscle by the tubercles was noted only in the region of the elbow.

A careful study of the sections was made, and in none was caseation of the tubercles noted. Inoculation of guinea-pigs with tissues and fluid repeatedly failed to yield the tubercle bacillus. It was never possible to demonstrate the tubercle bacillus in properly stained sections of tissue.

We have not been able to find a record of a similar case in the literature. Faulkner<sup>4</sup> in 1931 reported the case of a woman of 49, with a loose, firm, small body in the knee joint. The microscopic picture was considered to be that of a sarcoid growth.

A good article for orientation on sarcoid is that of Goeckerman<sup>5</sup>. Sarcoid is best known as a cutaneous condition, especially of the Boeck type. Recently the visceral complications of sarcoid have been stressed, and Goeckerman noted that splenomegaly, infiltrations of the finer bronchioles of the lungs and fibrocystic changes in the bones may accompany sarcoid of the skin. It is striking that our patient presented no cutaneous evidence of sarcoid at any time. There was no splenomegaly, but a roentgenogram of the lungs showed a hilar adenopathy. The osseous changes of sarcoid have been stressed most by Jungling, who termed the condition *ostetis tuberculosa multiplex*, more recently articles on sarcoid of bone have appeared by Bayer,<sup>6</sup> Van Alstine and

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<sup>4</sup> Faulkner, D. M. Primary Synovial Membrane Tumors of Joints, Surg., Gynec. & Obst. **53** 189, 1931.

<sup>5</sup> Goeckerman, W. H. Sarcoids and Related Lesions. Report of Seventeen Cases, Review of Recent Literature, Arch. Dermat. & Syph. **18** 237 (Aug.) 1928.

<sup>6</sup> Bayer, W. Osteitis tuberculosa multiplex cystica mit Sarkoid und Hilusdrüsenbeteiligung, Jahrb. f. Kinderh. **138** 31, 1933.

ment is usually bilateral and is characterized by the presence of repeated effusions within the knee joint, with thickening of the synovial lining. Aspiration may diminish the effusion temporarily, but there is a marked tendency for rapid recurrence. Only the knee joint is involved, and no definite cause can be invoked. Trauma is apparently coincidental. The reaction to tuberculin is negative, and no signs of syphilis are present. The Wassermann reaction of the blood and of fluid from the joint is negative. These cases form a baffling group, not so much from the standpoint of therapy as from the standpoint of etiology. Possibly, some occult focus of infection exists in the body. It is always necessary to rule out a specific lesion, although the clinical behavior of the knee joints in these cases resembles that of syphilis more than that of tuberculosis. Sundt<sup>13</sup> and Gill and Orr<sup>14</sup> described this type of case accurately.

Two cases of this particular disease group are included in this report, one in a youth of 18 and the other in a girl of 12 years. Each case is interesting enough for separate description. The value of arthroscopy lies in the clear examination of the joint and the possible therapeutic effect of lavage. It is possible to rule out tuberculosis by examination of the joint and by removal of a specimen for biopsy. Other suspected lesions are easily ruled out, and the disease process is seen to be confined to the synovia.

CASE 4—Alice S., a girl aged 12 years, fell and hurt her left knee while skating five years before she was admitted to the hospital. The knee was said to have been swollen, tender and discolored, but the condition cleared up after two weeks. The patient had scarlet fever in 1932, but no joints were involved as a sequel of the disease. Her left knee became swollen in October 1933, again after skating, although this time she did not suffer a fall. The left knee became progressively swollen, and at times it seemed hot and tender to touch. The pain was located on the inner side of the knee, was worse in the morning and was relieved by walking. Some limitation of motion was noted due to pain. No general symptoms, except possible excessive sweating in her sleep, had been noted. Another fall on the knee was noted, although the date of its occurrence was not remembered.

The child was well developed and seemed to be in perfect health. General examination gave entirely negative results. The left knee showed a large effusion, with some synovial thickening. Motion was free. The right knee which had always been free from disability, according to the patient, showed a smaller effusion. Its motion too was free. No tenderness existed in either joint. Serologic

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13 Sundt, H. The Diagnosis and Frequency of Tuberculous Disease of the Knee, *J. Bone & Joint Surg.* **13** 740 1931, Ueber Gonitis incertae causae insbesondere Synovitis chronica "simplex," unter besonderer Berücksichtigung des "Rheumatismus tuberculosus-Poncet" und Fallen von Synovitis mit ausgesprochener fleckiger Atrophie, *Acta orthop. Scandinav.* **3** 97, 1932.

14 Gill, A. B., and Orr, T. E. Chronic Synovitis of the Knee with Persistent or Recurring Effusion and of Undetermined Etiology, *J. Bone & Joint Surg.* **16** 159, 1934.

hypertrophic synovitis of the knee joint was made, and arthroscopic visualization was advised to determine if the proper time for synovectomy was at hand. Examination was made on May 11, 1932, and a good view was had of the enlarged fat pads and tremendously hypertrophied but very inflamed synovia. It was therefore advised that synovectomy be postponed, in view of the acuteness of synovial inflammation. A cast was applied to the limb.

The patient wore the cast for a month and then received vaccine therapy for fifteen weeks, without much improvement. Pain developed in her right hand and right shoulder. She had also received thorough treatment privately. It was thought that the acute condition of the joint was passed and that synovectomy should be done. On October 12 the operation was performed. At operation the peculiar and interesting feature of the joint was the presence of whitish deposits

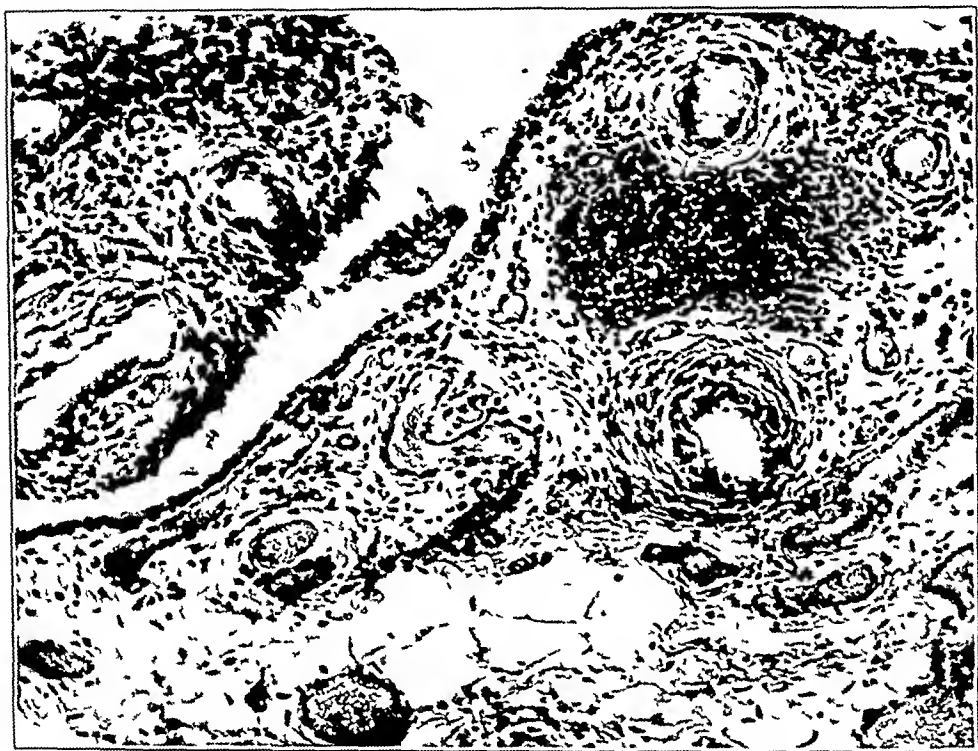


Fig 7 (case 2) —A section of synovial membrane, showing the reactive bodies

over the synovia, over the menisci and over some part of the cartilage, which resembled deposits of urate. The synovia was greatly hypertrophied otherwise, and the fat pads were much enlarged. The cartilage was in a good state of preservation. The synovia, fat pads and menisci were removed. On November 11 it was necessary to manipulate the knee to increase its range of motion. Otherwise, convalescence was uneventful. It should be noted that the white blood cell count just before the operation was still elevated to 16 800 with 67 per cent polymorphonuclears.

Chemically, the whitish deposit was definitely not urate but protein. The pathologic picture of the excised synovia was described as follows. There was slight hypertrophy of the synovial cells, with a slight tendency to the formation of villi. A general increase in vascularity existed, with lymphoid infiltration,

The effusion within this knee disappeared rather quickly, so that when the patient was discharged, on December 27, the knees seemed normal. On Feb 14, 1934, a note made in the clinic testified to the objective normality of her knees. On April 11, despite a fall on the knees three weeks before, they were still without further pathologic changes.

It cannot be said that this patient is cured, and only time will tell if recurrence of the effusion takes place. The effectiveness of therapeutic lavage is demonstrated here. The history of trauma is confined to the left knee, yet both knees were involved. We believe that the trauma was coincidental.

CASE 5—Jacob C, a youth aged 18, was first admitted to the hospital in 1928, because of questionable tuberculosis of the tendon sheath of the tibialis posterior tendon. Recovery was uneventful, and the tuberculous nature of the swelling about the tendon was never demonstrated. The knees were normal at this time. The patient's present illness, swelling of both knees, came on about three weeks before he was admitted to the hospital on Dec 18, 1933. On waking in the morning he noted that his knees had become swollen. He had had no previous illness recently, and no injury was recalled. The swelling of the left knee was marked, whereas the right knee was only slightly swollen. No pain and no tenderness were noted. He had lost about 4 pounds (2 Kg) since the onset of his illness. About 150 cc of fluid was removed from the left knee, but the effusion quickly returned.

The patient was tall and thin and walked with a definite knee limp. The left knee was full of fluid. Extension was possible to an angle of 165 degrees, and flexion to an angle of 75 degrees. The right knee on standing was held in a position of 175 degrees of extension, and extension was not possible beyond this point. Flexion of the right knee was possible to 55 degrees. No redness, heat or spasm was noted about either knee. No swelling of the sheath of the tibialis posterior muscle was noted. The patient's general health was good, and examination of the other systems of the body gave negative results.

Roentgenograms of both knees failed to show abnormalities. The Wassermann reaction of the blood was negative. The reaction to tuberculin was also negative. The sedimentation time of the blood was slightly increased. Repeated examination of the synovial fluid gave negative results culturally, and inoculations in guinea-pigs gave no evidence of tuberculosis. The Wassermann reaction of the fluid of the joint also gave negative results.

In the attempt to prepare the left knee for arthroscopic examination frequent aspirations of the knee were done. It was never possible, however, to reduce the effusion materially because of the rapid accumulation of fluid within it. It was finally decided to perform an arthroscopic examination of the right knee on the basis of the similarity of the pathologic process in each knee and to give the left knee lavage for any therapeutic effect it might have. The visualization of the right knee was excellent and demonstrated the synovial hypertrophy quite well. A small area of erosion on the under-surface of the patella was well brought out with eosin. Lavage to the left knee was given with over 500 cc of physiologic solution of sodium chloride. A biopsy specimen from the right knee indicated the presence of subacute synovitis.

Lavage of the left knee had no effect on the magnitude of the effusion, for it was necessary to aspirate the knee frequently. The right knee showed about the same amount of fluid as was present before arthroscopic visualization. Hence,

which was attached near the region of the internal meniscus. Several smaller masses were felt in the outer part of the quadriceps bursa. Tenderness was present over several synovial points. Flexion was limited to an angle of 90 degrees, and extension exceeded the normal limit of 180 degrees by 5 degrees. The right knee showed similar hyperextension.

The Wassermann reaction of the blood was negative. The reaction to the complement-fixation test for gonorrhea was 3 plus. The reaction to the tuberculin test was negative with all diagnostic dilutions. Roentgenograms showed the absence of a joint body, and the suprapatellar pouch was divided into two compartments. A sample of synovial fluid did not show organisms, and a culture was sterile. Some lymphocytes, polymorphonuclear cells and red cells were noted in a smear.

Repeated aspiration of the knee was done before arthroscopic examination. Good visualization was had of the knee in the extended position. Visualization was not possible with the knee in the flexed position because of extensive synovial hypertrophy. Tremendous masses of fat were seen, which were irregularly placed but were greatest in the region of the fat pads. The fat pads were somewhat enlarged and were fuzzy on their inner surface. The quadriceps pouch was short and showed a tremendous formation of villi. The patella seemed normal. This extreme degree of synovial overgrowth within the joint seemed to justify a diagnosis of lipoma arborescens. Several specimens were taken for biopsy, since such an overgrowth of the synovia is occasionally caused by tuberculosis adjacent to the synovia. The pathologist was of the opinion that the fatty masses removed for biopsy had come from para-articular tissues and not from the joint itself. The patient sustained some irritation from the arthroscopic procedure, as indicated by increased effusion within the knee, local heat over the joint, and a reaction of the temperature, which, going to 102 F. on the second day, vacillated between 99 and 101 F. for the third, fourth and fifth day postoperatively.

Arthrotomy was done two weeks later, on Feb. 28, 1934, and the arthroscopic observations were verified in their essentials. Synovectomy was done, and the fat pads and both menisci were removed. The menisci were degenerated, and a pannus was present at the edges. The postoperative course was not eventful.

The pathologic observations were most interesting. Grossly, the specimen consisted of the quadriceps pouch, the two menisci and two other pieces of synovia removed from the knee. All the pieces had undergone a more or less uniform pathologic transformation. The essential change was the appearance of smaller or larger pedunculated, polyp-like masses attached to the synovial lining by short, thin stalks. The polyps were in a sense growths or outgrowths of the tissue below the lining of the synovial membrane. Aside from the striking polypoid appearance, the synovia bore the evidence everywhere of abnormal change in the same direction. In some places, there were fine, delicate villi. In other places, shining through the synovial membrane, there were tiny, whitish but flat nodule-like nodules. At one point in the subsynovial layer of the pouch a whitish, cartilaginous mass about 1 cm. in diameter was seen. This mass was partly discolored by brown pigment. In fact, all of the resected synovia was considerably discolored by hemosiderin pigment, which may possibly be associated with the innate character of the lesion. Fibrin was noted in some areas.

Microscopically, numerous large pedunculated outgrowths of the joint capsule lined by synovia were observed. The dominant cells were those with a small oval nucleus and with indistinct cytoplasm. These were for the most part massed closely together in enormous numbers. A striking feature was the development in more than a few places of intercellular matter, which was probably hyaline,



described sixty-nine cases of osteochondritis dissecans, in three of which the site was in the external condyle

CASE 6—R H, a Negro aged 17, was first seen on Aug 17, 1933, because of a gradual swelling of his left knee, which had been manifest for six weeks and which had not been induced by any known trauma. No pain had been complained of. Frequently the patient felt that something was slipping on the inner side of his knee, but no real locking had taken place. Simple straightening of the leg removed this sensation. Examination revealed moderate effusion within the left knee joint. On the inner side, medial to the patella and just above the line of the internal meniscus, a pea-sized body was felt, which could be slipped in and out. This manipulation was painful. Motions of the knee were normal. After the aspiration of 75 cc of a yellow-brown, syrupy fluid, this body was more easily palpated.

In view of the history and physical findings, a presumptive diagnosis of osteochondritis dissecans was made. Yet the presence of the body near the internal meniscus suggested also the much rarer possibility of a tumor, such as a fibroma or a xanthoma, arising from the internal meniscus.

The patient was admitted to the Hospital for Joint Diseases on August 21. The joint body had slipped into the joint space the day before admission, in fact, it could no longer be palpated. There was now no effusion. On motion of the knee the synovia gave forth rustling and crackling sounds, indicative of the presence of synovitis. No tenderness was present over the region of the internal meniscus or elsewhere within the joint.

A roentgenogram of the knee gave no indication of foreign body or other intrinsic disease of the joint. The systematic examination of the synovial fluid also gave essentially negative results, this examination included a Wassermann test and culture of the fluid and inoculation of a guinea-pig. The smear of the fluid showed occasional red blood cells and white blood cells. The Wassermann reaction of the blood was also negative.

Arthroscopic visualization with the patient under general anesthesia and immediate arthrotomy were done on August 23. Unfortunately, because of a faulty electrical connection, it was necessary to interrupt the arthroscopic examination after a few minutes' examination. Small, continuous shocks were felt by the operator, and the patient experienced one involuntary but painless stimulation of his knee into extension. Yet, even in the brief time of examination, it was possible to note through the usual external puncture that the cartilage of the internal condyle of the femur was intact, that the internal meniscus was normal, that the patella was normal and, finally, that the quadriceps bursa was the seat of a definite and moderately advanced chronic synovitis.

Before the joint was opened, 20 cc of a 0.05 per cent aqueous solution of eosin was injected into the joint, and 15 cc of this was obtained by immediate aspiration. The usual median parapatellar incision was made. A striking and unusual picture of disease was now seen. The synovia of the bursa was moderately inflamed and fuzzy and presented a definite villous synovitis of from mild to moderate degree. The synovia was stained a light pink by the dye. The infrapatellar fat pads were slightly enlarged but not injected. The ligamentum mucosum was a reddish, somewhat inflamed band of tissue. Near the junction of the midportion and the upper portion of the external condyle a square erosion in cartilage about  $\frac{3}{4}$  inch (2 cm) square was noted, demarcated from the surrounding normal white cartilage by a light brown border of loose cartilage about

although suggestions of osteoid were not lacking. A moderate number of epulis-like giant cells, lymphocytes and fat-laden phagocytes were noted.<sup>12</sup>

A diagnosis of multiple, polypoid livalizing, connective tissue outgrowths of synovial membrane (fibroma) was made.

When discharged several weeks after the operation the patient was able to flex her knee to 90 degrees. There was still some swelling of the knee. In August 1934 she had no symptoms. There is still atrophy of the quadriceps muscle. Crepitation is present on motion, and flexion is limited to 85 degrees. Extension is full.

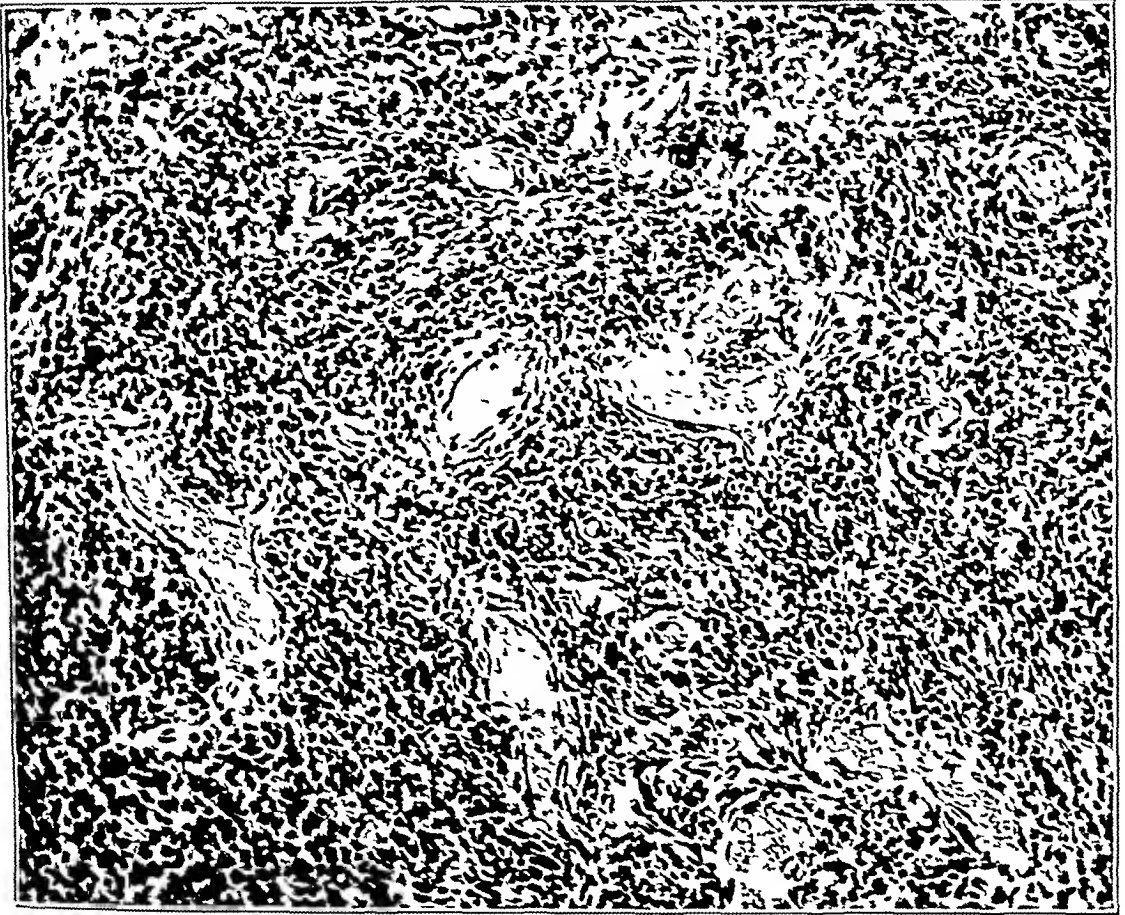


Fig. 10 (case 3)—A high power magnification of a tumor nodule.

#### CHRONIC NONSPECIFIC SYNOVITIS OF THE KNEE JOINT IN YOUNG PATIENTS

There is a typical disease entity of the knee joint in young patients which is perhaps best expressed by the foregoing title. The involve-

<sup>12</sup> The report also read: "Groups of very large pale reticular cells with small more or less centrally placed round nuclei, are seen. They apparently represent the intracellular accumulation of lipid."

proceeded satisfactorily, and it was not necessary to manipulate the knee at any time

On September 13 an unsuccessful attempt was made to visualize the lateral vessels of the knee by the closed method of arteriography, as advocated by Leriche. A cuff was tied just below the knee to prevent the passage of the contrast medium (thorium dioxide) below the leg. The femoral artery was felt slipping away from the needle, and it was not possible to enter it. Instead, a vein was entered, and some of the fluid refluxed into the abdominal veins. Roentgenograms made twelve seconds and four minutes, respectively, after the injection showed no abnormality. It was intended to determine if an embolic block existed in the lateral vessels of the knee.

The fact that the erosion in the cartilage did not reach to the bone apparently speaks for a factor acting locally, such as an unnoted trauma acting on the external condyle of the femur when the patella abutted against it in flexion and external rotation of the knee. In some persons the knees in the flexed position expose a large part of the femoral condyles, and even without patellar contact it may be possible to exert direct trauma to the cartilage. Yet it is well known that it is most difficult to fracture normal cartilage, even with a strong blow.

The irritation of the joint bodies created a state of chronic synovitis. This synovitis does not necessarily disappear after the removal of the joint bodies, and occasionally it may be advisable to remove the diseased synovia by synovectomy. The remaining portion of the ulcer in the cartilage is said to fill in with fibrous tissue or fibrocartilage, so that ultimately only a small depression is noted at the site of the disease. It is of course well known that cartilage does not heal over well. Clinically, this is also true, and these joints must always be considered as subnormal, with the ever present possibility of the development of arthritis sooner or later. In experimental animals a defect in the cartilage often leads to widespread arthritis. This was proved by the work of Kev,<sup>23</sup> and Burman and Sutro.<sup>24</sup> A long follow-up of patients with this condition should indicate a greater frequency of such arthritic changes.

The patient was discharged on September 14. On October 21 he stated that he was entirely cured. A belated roentgenogram of the spleen and liver made to determine the presence of thorium dioxide showed no abnormality. On October 24 it was noted that extension of the knee was full and that flexion was possible to 95 degrees. There was no swelling and no crepitation on motion. Good power was present in the quadriceps muscle. On December 26 the patient was able to walk an unlimited distance and was without symptoms. Extension was full, and flexion was possible to 85 degrees. The patient was last seen on April 20, 1934. His knee showed a slight limitation in extreme flexion but was normal otherwise. He could play basket-ball, run or walk without disability. He considered his knee to be entirely normal.

Microscopic examination of the excised cartilage and synovia did not help us from an etiologic standpoint. The cartilage showed hypercellularity of the superficial layers and some localized thickening of the perichondrium. The synovia showed some villous hypertrophy and was the seat of chronic synovitis.

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23 Kev, J. A. Experimental Arthritis. The Changes in Joints Produced by Creating Defects in the Articular Cartilage, *J. Bone & Joint Surg.* **13** 725, 1931.

24 Burman, M. S., and Sutro, C. I. Staining of Cartilage. Gross Staining by Intra-Articular Injection of Dyes in Animals, *Arch. Surg.* **27** 801 (Oct.) 1933.

tests for syphilis and gonorrhea gave negative results. The roentgenogram showed an essentially normal picture.

Examination of synovial fluid showed a moderate number of lymphocytes and polymorphonuclear cells. No bacteria were seen. The Wassermann reaction of fluid from the joint was negative. Culture of the fluid and inoculations of guinea-pigs yielded negative results for tuberculosis. The sedimentation time of the blood was at a high normal level.

Arthroscopic observation of the left knee was done on Dec 7, 1933. Visualization was perfect. An interesting lesion of the synovia was noted. Fringing each border of the patella were large, oblong villi, which presented an outer third of clear yellow and an inner, clearly demarcated two thirds of delicate rose-pink. The infrapatellar fat pads were slightly enlarged. Some synovial hypertrophy existed in the quadriceps bursa. At the base of the intercondyloid fossa and just anterior to it were a large number of small, petal-like villous structures, with the same type of coloring noted in the villi about the patella. These villi were fringed like coral, and their superior edges were thus slightly serrated. The joint cartilage was normal. The internal meniscus was well visualized and was normal. No specimen was taken for biopsy. Convalescence was uneventful, and the effusion within the knee did not return.

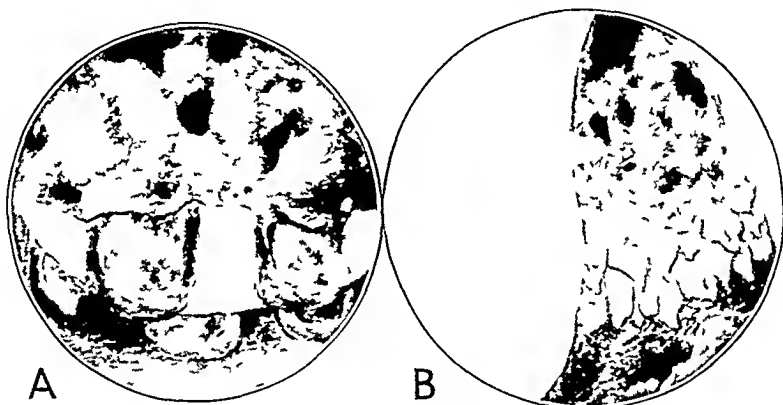


Fig 11 (case 4) — *A* is an arthroscopic view of the left knee joint, showing large, oblong-shaped villi fringing the patellar border. The outer third of each villus is a clear yellow and is clearly demarcated from the inner two-thirds which is rose pink. The cartilage of the under surface of the patella is normal. *B* shows a large number of coral-like villi, serrated at their tips, seen at the base of the intercondyloid fossa. They are colored as the oblong villi about the patella.

Arthroscopic examination of the right knee was done two weeks later. At this time no effusion was present in the left knee. The right knee joint was clearly visualized. The observations were in many ways similar to those seen in the opposite knee. The synovial villi about the patella were diaphanous and showed only a suggestion of the unusual coloring noted in the other knee. The oblong shape of the villi was noted. On the medial aspect of the joint there was a large collection of thickened and roughly oblong villi, so that visualization of the internal meniscus was incomplete. The suggestion of the unusual coloring was noted here too. The base of the intercondyloid fossa did not show the synovial villi noted in the left knee. Otherwise, the observations on the rest of the joint corresponded with those on the left knee. The biopsy specimen showed the presence of non-specific chronic synovitis.

may have a soft, thick or even semifluctuant feel, so that its growth beneath the patella in the case of Nodet<sup>31</sup> gave the impression of pseudobalottement. The tumor may slip in and out of the joint on motion, or it may be forced manually into the joint. The location varies, though it is often located near the alar ligaments. It may arise from the quadriceps bursa or it may be felt in the popliteal fossa. In Herhold's<sup>29</sup> case, the tumor was attached by a pedicle to the anterior cruciate ligament. Motion of the knee joint is usually not limited, but in Auvray's<sup>32</sup> case flexion was limited to 90 degrees both actively and passively.

While the presence of the tumor is confirmed at operation, the small incision used for its removal does not allow an adequate survey of the entire joint, so that many authors, while mentioning synovial irritation as a possible etiologic factor, made no note of the state of the synovia. In Zullig's<sup>33</sup> case a lipoma was removed at one point within the joint, but it recurred at another point.

Mixed tumor may occur. The tumor may be both intra-articular and para-articular, as in Campbell's<sup>34</sup> case. However, in this case the diagnosis was roentgenologic, and the supposed masses of fat, which cast a dense shadow on the roentgenogram, were not verified by opening the joint. Malignant change to liposarcoma took place in Auvray's<sup>32</sup> case, and Blagovieshtshenski<sup>35</sup> was cited by Auvray as having described a case of liposarcoma of the knee joint. We do not know whether the growth was a solitary tumor.

The tumor in the case of Simon,<sup>36</sup> which is considered to be the first case described, was apparently not a lipoma but a fibroma. Volkmann,<sup>37</sup> then, is to be given priority for the first description of solitary lipoma of the knee. Filter,<sup>26</sup> Otterbeck,<sup>25</sup> Annandale<sup>38</sup> Barwell,<sup>39</sup>

31 Nodet, V. Le faux choc rotulien dans un cas de lipome du genou, *Province med*, Lyon **10** 492, 1896.

32 Auvray. Lipo-sarcome primitif intraarticulaire du genou, *Bull et mem Soc de chir de Paris* **46** 534, 1920.

33 Zullig, J. Tumoren der Kniegelenkkapsel, *Cor-Bis schweiz Aerzte* **47** 1368, 1917.

34 Campbell, D. Intra- und extraartikuläre Lipome des Kniegelenks, *Fortschr, a d Geb d Rontgenstrahlen* **37** 852, 1928.

35 Blagovieshtshenski, D. A. Dendroid Lipomatous Tumor of the Knee Joint, *Khirurg Arkh Velyaminova* **27** 653, 1911.

36 Simon, G. Exstirpation einer sehr grossen, mit dickem Stiele, angewachsenen Kniegelenkmaus mit glücklichem Erfolge, *Arch f klin Chir* **6** 573, 1865.

37 Volkmann, quoted by Stieda<sup>24</sup>

38 Annandale, T. An Address on Internal Derangements of the Knee Joint and Their Treatment by Operation, *Tr Med-Chir Soc Edinburgh* **6** 78, 1886-1887.

39 Barwell, quoted by Annandale<sup>38</sup>

three weeks later a synovectomy of the left knee was done. Pathologic examination of the excised tissue revealed nonspecific chronic synovitis. An interesting sympathy was noted in the subsidence of the effusion of the right knee after the synovectomy of the left knee. Symptoms in the right knee also disappeared. The patient was discharged on March 6, 1934.

It was necessary to admit the patient again in the latter part of October because of the recurrence and persistence of fluid in the right knee. A synovectomy was done on this knee.

An interesting point in the history during the interval related to a transient swelling of one sternoclavicular joint in June. This swelling subsided promptly without treatment. No evident focus of disease has been found. The patient has been followed up regularly in the outpatient-department. Motion in both knees is good, albeit with slight limitation in flexion. Fluid has recently reappeared in the left knee (April 1935) controlled by a simple compression bandage. One disturbing feature has developed, epididymitis of unspecific origin. The patient gets about well and wishes to go to a camp of the Citizens' Conservation Corps.

It is important to differentiate the condition in this group of cases from specific disease of the knee joint and from those nonspecific diseases of the knee joint which simulate a specific disease and are accompanied by local inflammation or the definite signs of the disability of the knee after trauma. This group is limited to a small percentage of cases of involvement of the knee. A long follow-up in this type of case may ultimately disclose involvement of other joints, the usual nature of the arthritic process being delayed or masked by the predominant disease of the knees.

#### OSTEOCHONDRITIS DISSECANS

Case 6 was noteworthy because of its unusual features and because of certain points of view regarding etiology and treatment which it brought up. Although Conway,<sup>15</sup> Fairbank,<sup>16</sup> Balensweig,<sup>17</sup> Filippi,<sup>18</sup> Delchef,<sup>19</sup> Heine,<sup>20</sup> and Niessen<sup>21</sup> described cases of osteochondritis dissecans of the external condyle of the femur, in none was there a location of the disease process similar to that in this case. Hellstrom<sup>22</sup>

15 Conway, F. M. Osteochondritis Dissecans, *Ann Surg* **99** 410 (March) 1934.

16 Fairbank, H. A. T. Osteochondritis Dissecans, *Brit J Surg* **21** 67, 1933.

17 Balensweig, I. Osteochondritis Dissecans of the Knee, *J Bone & Joint Surg* **7** 465, 1925.

18 Filippi, G. Contributo allo studio della osteocondrite dissecante (Konig), *Chir d'org di movimento* **16** 35, 1931.

19 Delchef, quoted by Fairbank.<sup>16</sup>

20 Heine, J. Beitrag zur Pathogenese der Osteochondritis Dissecans, *Deutsche Ztschr f Chir* **206** 119, 1927.

21 Niessen, H. Ueber symmetrische Osteochondritis dissecans der lateralen Femurcondylen, *Beitr z klin Chir* **143** 159, 1928.

22 Hellstrom, John. A Few Experiences in Reference to Osteochondritis Dissecans, *Acta chir Scandinav* **74** 427, 1934.

excursion. It was located at the lower pole of the patella. It was thought that the tumor might come from the external fat pad, although it seemed to be placed too high. Slight atrophy of the quadriceps muscle was present. Motions of the knee were complete but crepitant. The left knee also showed crepitation on motion.

Both feet, especially the right, were painful, and without shoes, the patient walked with a perceptible limp. There was marked atrophy of the muscles of both calves, so that the patient could not stand on tiptoe well. Tenderness was present over the tuberosity of the fifth metatarsal bone of the right foot, just behind the tuberosity and over the entire shaft of the fifth metatarsal bone. Tenderness was also present over the external aspect of the ankle and over the medial aspect of the heel. The metatarsal heads were also tender. The peroneal tendons were slightly taut. Inversion of the foot was limited, and subastragaloid motion was definitely painful and limited. Forced inversion increased the pain, especially in the region just behind the tuberosity of the fifth metatarsal bone. Some swelling was present around the ankle joint, around the subastragaloid joint and in the region of the ball of the foot. Dorsiflexion of the foot was possible to an angle of about 90 degrees. Mild pronation of both feet was present.

A general and neurologic examination of the patient gave negative results. A roentgenogram of the right knee showed no abnormality. A diagnosis of gonorrheal arthritis of both knees and both feet was made. The tumor was considered to be either a lipoma or a fibroma, probably the former.

The tumor, which was removed with simple local anesthesia a few days later at the Hospital for Joint Diseases, arose from the region of the lower pole of the patella as a discrete mass of fat which slipped in and out of the joint, as noted on examination. There were marked hypertrophy and some inflammation of the synovia and fat near the fat pads. The synovia in general was definitely abnormal, in that it was red and hypertrophic in places. The joint cartilage was normal. Both fat pads were slightly enlarged. The external meniscus was normal. It was rather difficult to remove the tumor because it had not been transfixed. It was a true lipoma the origin of which was the external alar ligament.

The postoperative course was not eventful. Microscopic examination of the excised tumor proved its lipomatous nature. On May 29, nineteen days after the operation, the patient walked 7 miles (43 kilometers). On June 7, the right knee showed full motion and less crepitation than before. The tumor was no longer palpable. No complaints were referable to the knee.

CASE 8—The patient was a Negress, aged 39, who until seven months before her visit to the clinic was perfectly well. At this time, she fell while walking, striking her right knee. Pain was very mild at first, but this gradually increased in severity. The knee, which had become swollen at the time of the accident, remained swollen, and at the end of a month the knee was somewhat stiff. A month after this, the patient noted a lump in her knee, which moved about with motion of the knee. She had been able to climb stairs and to walk on uneven ground only by holding the knee stiff.

The right knee was about  $\frac{3}{4}$  inch (06 cm.) larger in circumference than the left and showed a small effusion. A rounded mass was felt on the medial aspect of the patella, which slipped in and out of the space between the patella and the internal condyle of the femur as the knee was flexed and extended. The mass measured 1 by  $\frac{3}{4}$  inch (25 by 2 cm.) and was smooth, rounded and definitely firm. In the course of its slipping it produced temporary locking, causing temporary severe pain. In the flexed position of both knees at an angle of 150 degrees mild lateral instability was present, with some bony grating.

$\frac{1}{16}$  inch (0.15 cm) wide. Within this erosion the base of which was not bone but an irregularly papillated cartilage, were two free fragments of normal-appearing cartilage of equal size. The dye had stained the eroded area a light pink, whereas the normal cartilage had not been stained. The cartilage of the internal condyle was normal, and no area of dissection was noted in it. In addition, a red fibrous membrane of heavy pannus spread out from the anterior cruciate ligament and attached itself along the free border of the internal meniscus along its entire length. Beneath this and over the internal condyle of the tibia, another square piece of white cartilage, about  $\frac{3}{4}$  inch square, was noted. Another body, the size of half a pea, was observed between the outer part of the external condyle of the femur and the lateral synovial expansion. Both menisci were intact.

Both free bodies were easily removed from the ulcer in the cartilage in the external condyle. The loose brownish border was excised at its junction with normal cartilage. The small body laterally was also removed. A slit was made in the reddish membrane, and the body over the internal condyle of the tibia was

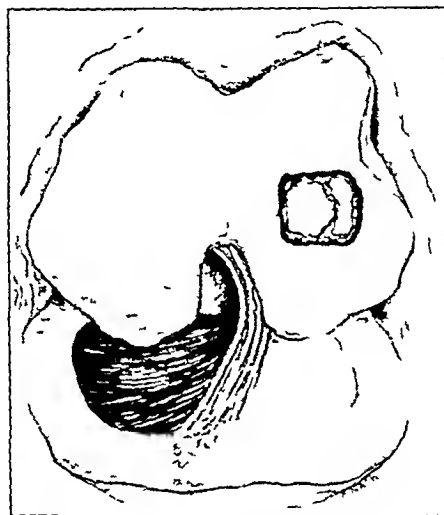


Fig 12 (case 6) —A drawing of the opened knee, illustrating the pathologic changes noted in the knee. The ulcer of the external condyle of the femur, with its two pieces of cartilage, is evident. The reddish, fibrous pannus extends from the anterior cruciate ligament to the internal meniscus, attaching along the entire free border. It covers over another loose piece of cartilage the origin of which is probably from the internal condyle of the tibia.

taken out. Its origin, presumably from the internal condyle, could not, however, be verified by direct inspection, since this would have necessitated a close dissection of the pannus, a thing which was not considered advisable. A synovectomy was done by which the synovia was removed from the bursa under the quadriceps tendon and its lateral expansions, and the inner fat pad was removed. The altered ligamentum mucosum was not touched.

The wound was closed in layers, and a cast was applied from the toes to the groin. Convalescence was uneventful, the highest peak of temperature being 101.4 F. By the twelfth day there was no further rise from the normal. The cast was removed soon afterward, and active motion of the knee was begun. This



present about the knee. The patient felt the knee to be weak and therefore used crutches. On April 7 the angle of greatest extension was 180 degrees and the angle of greatest flexion was only 90 degrees. Attempt at further flexion was painful. In November 1934 the knee was no longer swollen, but it was still crepitant on motion. Flexion was almost full. The patient still complained of some pain. On her last visit, on April 20, 1935, she complained of pain in her knee on going up and down steps and in rainy weather. She walked with a slight right-sided limp. Motion was complete but slightly crepitant. The patient was satisfied with the end-result.

#### SYMPATHETIC SYNOVITIS OF THE KNEE JOINT ARISING FROM AN ADJACENT BONY FOCUS

CASE 9—Le Roy D., a Negro aged 15, was seen in the clinic on Dec 5, 1933, because of a swelling of his right knee, which had appeared recently without trauma. A year previously he had noted a similar swelling, which had promptly subsided. Examination of the joint after aspiration of 150 cc of yellow synovial fluid gave essentially negative results. A Wassermann test of this fluid caused a reaction of 4 plus. On December 9, 60 cc of synovial fluid was aspirated, on this occasion and on two other occasions shortly after that the Wassermann reaction of the fluid was negative. The Wassermann and Kahn reactions of the blood were also negative. The reactions to tuberculin were negative. This thorough serologic check-up caused us to discard a presumptive diagnosis of syphilitic arthritis. The patient was admitted to the Hospital for Joint Diseases on Jan 15, 1934, because of disability of the knee. Slight pain was complained of, and some limitation of motion due to the accumulation of fluid was noted.

The patient walked with a mild right knee limp. The knee could not be extended fully, and the angle of greatest extension was 175 degrees, whereas the angle of flexion was 60 degrees. A patellar ballottement was present, and some periarticular thickening was noted. No tenderness was present in or about the joint. Definite pain was complained of over the tibia about 3 inches below the level of the joint line, especially about the posterior portion of the tibia. The muscle of the calf was tender. Heat and some swelling of the soft tissue were felt over the tibia, especially posteriorly. Tenderness was very marked about 4 inches (10 cm) below the joint line, and a mass could be felt on the inner side of the tibia.

The latter findings had not originally been noted, nor were they present at the previous examination. A roentgenogram of the right knee, which had been made in the clinic, had been interpreted as showing no abnormalities, but on reconsideration at this time there was seen in the lowermost part of the tibia represented on the film, about 3 inches below the knee joint, a peculiar shadow of sclerosis. Other roentgenograms, which visualized the entire tibia, showed circular areas of density in the proximal one third of the bone projecting into the medullary cavity from the posterior portion of the substantia compacta. Sclerotic borders defined fairly well these areas of density. The cortex at the junction of the proximal and middle two thirds of the shaft was distinctly thickened. The periosteum was normal. The medullary cavity showed no further changes. No formation of new bone was noted in the soft parts.

A clinical diagnosis of abscess of the bone of the tibia was made, while a roentgenologic diagnosis of hemorrhagic osteomyelitis was given. The synovial effusions appeared to be due not to any intrinsic disease of the joint but to a sympa-

## SOLITARY LIPOMA OF THE KNEE JOINT

We have had the opportunity of observing two cases of solitary intra-articular lipoma of the knee joint. This is an uncommon tumor of the knee joint the primary clinical importance of which lies in the fact that it acts as a mechanical block to motion producing repeated temporary locking. It is our opinion that the solitary lipoma arises in the presence of other diseases of the synovia and that it is such synovial irritation which rarely allows a synovial villus to proliferate so that a true lipoma is formed. This corresponds in general with the ideas of Otterbeck<sup>25</sup> and Filter<sup>26</sup> and is in accordance with clinical observations. We do not take much stock in the theory of König that a solitary lipoma arises through rupture of the synovial membrane with intra-articular protrusion of subcapsular fat.

According to Stieda<sup>27</sup> only twelve cases had been described up to 1896, and since then less than an equal number have been reported in the literature. Geschickter<sup>28</sup> in a review of cases of lipoma and lipoid tumors, noted lipoma of a joint in seven of a group of seventy cases of lipoma of the breast and viscera. Occasionally, and in earlier reports, some confusion of a solitary lipoma with enlargement of the infrapatellar fat pads (Hoffa's disease) is noted.

While a history of direct trauma may be obtained such as a direct fall on the knee, it is most likely that the trauma came about either coincidentally or as a result of the interposition of the tumor between the bony surfaces of the joint. This certainly was true in our second case and was definitely proved in the case of Herhold,<sup>29</sup> in which the patient, a cannoneer, had noted a tumor before the gross trauma occurred which brought him to consult the physician. The tumor occurs at all ages and in both sexes. Pain is variable. It may not be present or it may be severe, especially at the moment of temporary locking. The swelling of the knee may be due to effusion to the presence of the tumor, to the presence of coexisting synovial disease or to a combination of these factors.

The lipoma may rest dormant or its gradual growth may interfere with motion. Its size varies, a maximum of 3½ inches (9 cm.) having been reached in the case of Hunt.<sup>30</sup> The tumor is well outlined and

25 Otterbeck, W. Freies Lipom im Kniegelenk, Inaug. dissert., Bonn, J. Bach 1892.

26 Filter, M. Ueber solitare Lipoma des Kniegelenks und ihre Ursachen, Inaug. dissert., Greifswald, J. Abel, 1890.

27 Stieda, H. Ueber das Lipoma arborescens des Kniegelenks und seine Bedeutung zu chronischen Gelenkaffektionen, Beitr. z. klin. Chir. **16** 285, 1896.

28 Geschickter, C. F. Lipoid Tumors, Am. J. Cancer **21** 617, 1934.

29 Herhold. Zur Frage des Lipoma Genu. Arch. f. klin. Chir. **52** 705, 1896.

30 Hunt, E. H. A Case of Lipoma of the Knee, St. Barth. Hosp. J. **9** 121, 1902.

Microscopically, spindle-shaped connective tissue cells were present as the predominant cell element, arranged compactly and often interlacing. Numerous drawn-out multinuclear cells were seen throughout sections of softer tissue. The discoloration of the tissue was due to blood pigment. A scattering of polymorphonuclear cells and mononuclear cells was seen. Some of the surrounding bone was sclerotic. The lesion in itself was not bone-forming. A pathologic diagnosis of an intramedullary fibrous tissue lesion, which might possibly be considered as a giant cell variant, was made.

The postoperative course was uneventful. Examination of the knee on February 1 demonstrated no patellar ballottement. On February 3 arthroscopic examination of the right knee was done to determine if any intra-articular lesion existed. Good visualization of the joint was obtained, and a moderate increase in fat was noted, especially in the form of large, irregular villi in the region of the fat pads. A thin, brown pannus was seen running vertically just above the intercondylar fossa. No other significant findings were noted. The synovial change was considered to be the result of repeated effusion.

The limb was kept immobilized in a cast for three months, at which time the patient was allowed up. On May 5, after he had been up and about for a month, a return of effusion was noted in the knee. About 20 cc was aspirated. The fluid was again aspirated, and on the last examination several months later fluid was still present in a small amount. The bony focus of disease was healing well.

As far as it can be determined in this case without actual arthrotomy, the effusion within the knee seems to have been due to the subjacent bony focus, a sympathetic synovitis. This condition is not uncommon and has occurred in many cases of juxta-articular lesions, including fracture, infection and tumor. Yet it was imperative here to rule out an actual lesion of the knee, and this was done by arthroscopic visualization.

Weir,<sup>40</sup> Stieda,<sup>27</sup> Fisher,<sup>41</sup> Wagner,<sup>42</sup> Lauenstein,<sup>43</sup> and Bland-Sutton<sup>44</sup> also described cases

The exact diagnosis is sometimes difficult, even if solitary lipoma is thought of. An exact preoperative diagnosis may be difficult, since a fibroma, a chondroma, a pedicled sarcoma, a xanthoma, an angioma, a pedicled sarcoma, a meniscal cyst or tumor, a synovial cyst or an ordinary rounded joint body may produce a similar picture of disease. The consistency of the tumor, the character of the synovial fluid, which may be bloody with angioma, xanthoma or sarcoma, may help in the diagnosis. A high value for cholesterol in the blood is not uncommon with xanthoma, and a determination of the cholesterol content of the blood should be carried out in every doubtful case. The presence of hypercholesteremia may be a guide to an exact diagnosis. The roentgenogram usually fails to show an abnormality, although it is possible that the fat may cast a shadow, especially if calcium is deposited within it.

Treatment is surgical and consists in the removal of the tumor. The tumor should be transfixed by two needles just before the synovia is entered, otherwise, it may be difficult to locate it properly. The ultimate fate of the joint rests on the coincident pathologic process in the joint.

CASE 7—Raoul D., a man aged 24, a Santo Domingan who had recently come to New York, was seen first on May 1, 1933, because of pain in his feet. While in Santo Domingo, one and a half years previously, he had gonorrhea, for which he was treated rather perfunctorily. He was in bed for three months because of the development of acute gonorrheal arthritis of the left knee. No treatment was given, and the disease subsided spontaneously. Motion in the knee was restored by active exercises instituted on the patient's own initiative. The right knee was not involved, according to his statement. He had received intravenous injections, apparently for syphilis, at another hospital. The gonorrheal urethritis was cured, but since getting out of bed the patient had had pain in both knees and both feet. He was given orthopedic shoes by a chiropodist, and two and a half weeks later he first noted a small tumor on the outer side of his right knee. This slipped in and out on motion. There was no trauma at any time to the knee.

A tumor the size of a dime was noted on the external aspect of the right knee joint. The tumor was not painful on pressure and had the consistency of thickened fatty tissue. It slipped in and out of the joint between the angle of 180 and that of 170 degrees of motion and caused neither pain nor temporary locking in its

40 Weir, R. F. On Fatty and Sarcomatous Tumors of the Knee Joint. *M. Rec.* 29 725, 1886.

41 Fisher, A. G. T. *Internal Derangements of the Knee Joint*, New York, The Macmillan Company, 1924.

42 Wagner, A. *Ueber Lipome des Kniegelenks*, Inaug. dissert., Königshütte, R. Giebler, 1887, quoted by Herhold<sup>29</sup> and Stieda<sup>24</sup>.

43 Lauenstein. *Centralbl. f. chir.* 11 1, 1884, quoted by Stieda<sup>24</sup> and Weir<sup>40</sup>.

44 Bland-Sutton, J., quoted by Herhold<sup>29</sup>.



Fig 1—Roentgenogram taken in May 1924 of a benign giant cell tumor in the upper portion of the right tibia

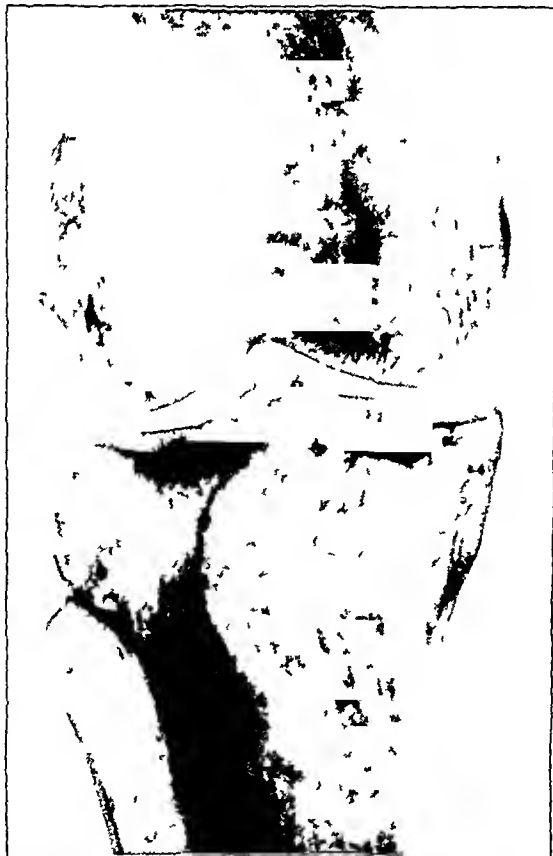


Fig 2—Roentgenogram taken in March 1935 of the right knee joint, showing the appearance of the site of a benign giant cell tumor eleven years after operation

General examination gave negative results except for a large uterine fibroid. Years ago she had received antisyphilitic treatment. Recently the Wassermann reaction of the blood had been negative.

A joint body, possibly a chondroma or fibroma, was thought of. It was also suggested, in view of the mild lateral instability with bony grating (in the flexed position), that a Charcot knee be considered. A roentgenogram of the knee did not show abnormalities, and this diagnosis was discarded.

On Jan. 24, 1934, an arthroscopic examination and arthrotomy were done. The arthroscopic procedure was done to determine the possibilities of visualization of such a tumor and also to determine the general state of the joint. Experience in the previous case had taught us to expect other intra-articular pathologic changes. Chronic villous synovitis was noted in the joint. The region of the fat pads and the bottom of the joint could not be well examined. The tumor on the medial aspect of the joint was visualized indistinctly, especially when it was forced into the joint on external pressure. Its edges could not be determined. Its surface was white with red streaks over it. The mass was much too large to be seen in one area of vision. In general arthroscopic examination of the joint was not very satisfactory.

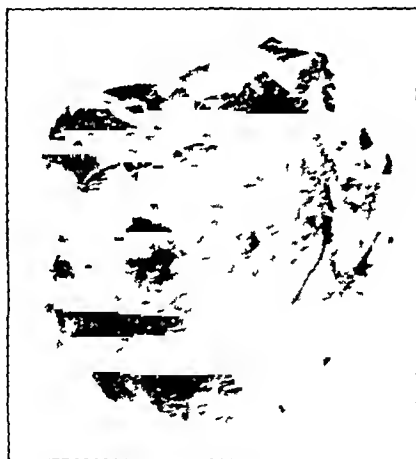


Fig. 13 (case 8) —A photograph of the lipoma removed from the knee joint.

The tumor was transfixed by two needles before the joint was entered and its removal was made easier by this transfixion. The tumor was encapsulated. It was the size of the yolk of an egg, and it entered the joint from the superior internal angle of the patella. Its exact point of origin was not determined through the small incision used for its removal. No note was made of changes in the synovia or of other pathologic change within the joint, and indeed the incision was much too small for a good view of the interior of the joint. The microscopic examination of the tumor showed an encapsulated growth of fatty tissue in the form of a slightly flattened disk 3.5 cm in diameter. Histologically, it was a lipoma.

The postoperative course was uneventful. It was difficult to establish motion because of severe pain in the knee and because of persistent swelling. A roentgenogram made on March 22 showed marked atrophy of the bones of the knee joint. The angle of greatest extension, both actively and passively, was 180 degrees, flexion was almost normal then. No definite points of tenderness were

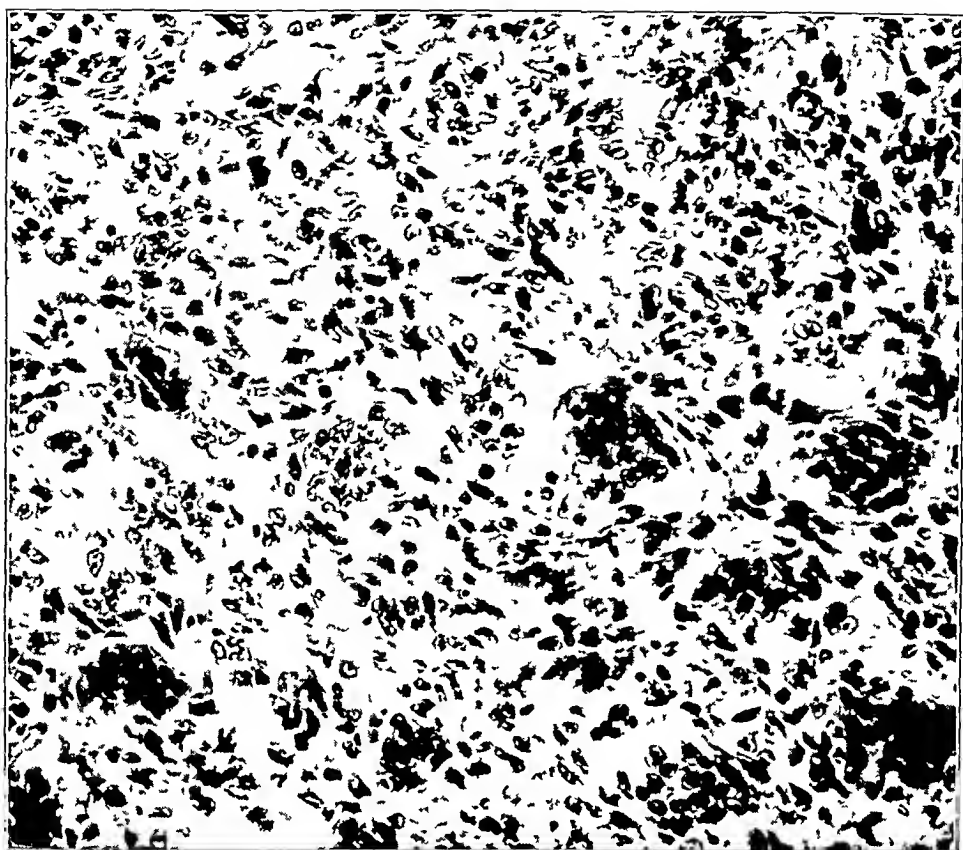


Fig 3—Photomicrograph of a section of a benign giant cell tumor removed in May 1934 Magnification,  $\times 300$

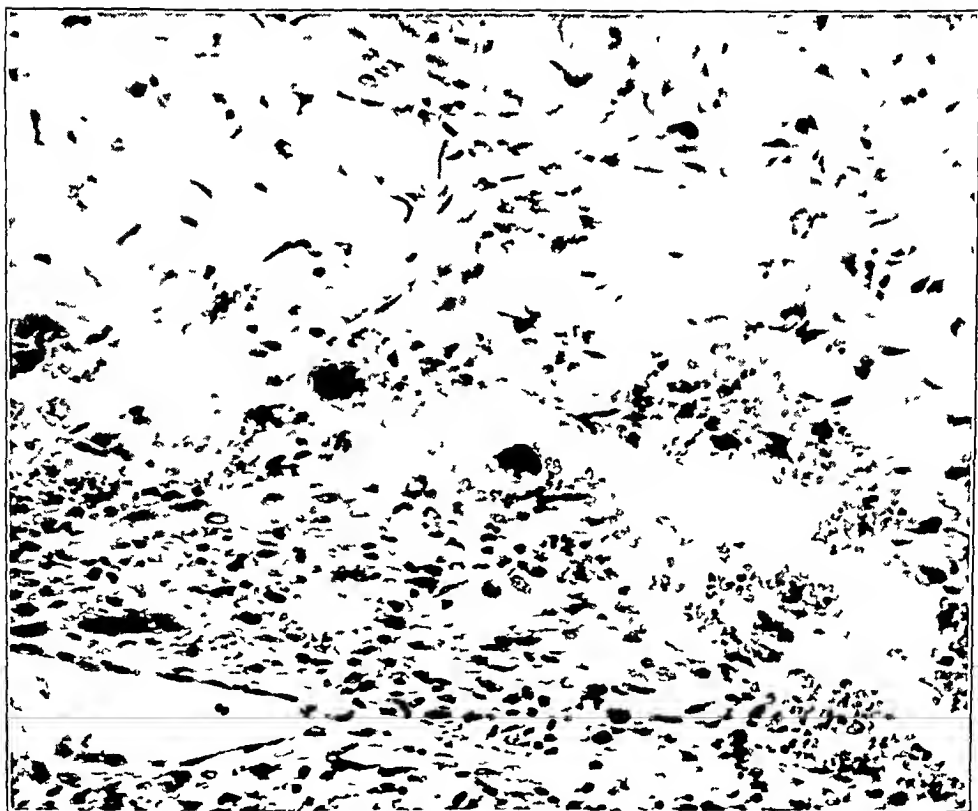


Fig 4—Photomicrograph of a section of dense fibrous marrow removed from the site of a giant cell tumor in March 1935 A focus of small foreign body giant cells is seen These are most likely a part of the chronic healing process, in which fibrous tissue is slowly being replaced by spongy bone and marrow Magnification,  $\times 300$

thetic irritation from the old but now active focus of disease in the bone. This opinion was held despite the distance of this focus from the joint, since no other diagnostic possibility presented itself.

Operation on January 17 by Dr. N. Ransohoff revealed a cystlike mass in the upper and outer posterior aspect of the tibia, lined with a raspberry-like membrane. Some fluid was encountered which looked like pus and which on smear showed a



Fig. 14 (case 9) —Note the cavitation in the posterior portion of the tibia. It is sharply demarcated by sclerotic bone. No evidence of adjacent periostitis is seen.

few pus cells but no organisms. An osteotomy was done. Culture of the tissues was sterile. A culture of one piece of bone was sterile, whereas a culture of a piece of another bone showed a micrococcus and a diphtheroid bacillus in forty-eight hours, these were probably contaminants.



# PARALYTIC DISLOCATION OF THE HIP

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AND

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The problem of therapy presented by paralytic dislocation of the hip causes every orthopedic surgeon many moments of uneasiness and doubt. Difficult as the treatment of this condition has always been, the dilemma in which the surgeons of an earlier generation found themselves could still be resolved more readily than that of the modern surgeon. In his review of the condition, Sever<sup>1</sup> divided cases of paralysis of the hip into three categories. The first group consisted of cases of the early stage, in which mild paralysis without dislocation existed. In these the prognosis was good, and the treatment consisted of the correction of deformities and the application of a plaster or a brace. The second group consisted of cases in which a reducible paralytic dislocation existed. The prognosis was not as good as that in the former group, but the treatment consisted of correction of the contractures and the application of a brace or a plaster. In the third group of cases, those of the irreducible paralytic dislocation, the prognosis was bad, and fusion was recommended after correction of the contracture. There was really no great problem, and no discriminating choice of procedure was either necessary or possible. But since the increase of the surgical horizon by means of the Jones operation, the Lorenz method of bifurcation, the Schanz osteotomy, the shelf operations described by Gill and Albee, the Dickson method of transplantation of muscle, etc., the choice of method has become serious and vital. The surgeon must constantly face the question whether conservative or radical treatment should be employed. In the event that operation is deemed necessary, he must determine whether mobility is invariably to be sacrificed in favor of stability or whether the effort to conserve both functions is justified.

From some of the reports in the literature the impression may be gained that the latter alternative is to be preferred to the former. Elzinga and Key<sup>2</sup> after a study of twenty-six cases, in eight of which an operation was performed, stated categorically "The operation recommended is the shelf operation." Jones<sup>3</sup> reported four cases in which the opera-

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From the Hospital for Joint Diseases, service of Dr Harry Finkelstein

1 Sever, J W Boston M & S J **165** 313, 1911

2 Elzinga E, and Key, J A J Bone & Joint Surg **14** 867, 1932

3 Jones, Ellis J Orthop Surg **2** 183, 1920

# SITE OF BENIGN GIANT CELL TUMOR ELEVEN YEARS AFTER OPERATION

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AND

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The literature contains few reports dealing with the sites of giant cell tumors long after operation, and there has been much curiosity as to the type of tissue filling the defects

Herendeen<sup>1</sup> reported a series of six cases observed for from five to ten years in which the diagnosis of giant cell tumor was made from roentgenograms only. After roentgen therapy the symptoms disappeared, but subsequent roentgenograms revealed considerable abnormalities still existing in the bony structure. Although varying degrees of filling in by cancellous bone had occurred several years after the patients first came under observation roentgenograms still showed a picture which was atypical of giant cell tumor. No biopsies had been performed during the follow-up periods.

The purpose of this report is to record an instance of benign giant cell tumor of the upper end of the tibia in which histologic studies were made on material removed at the first operation and in which material for histologic study was obtained eleven years later at a second operation, performed on the same region because of recurrent pain and persistent abnormal roentgenographic findings of reduced density at the site of the tumor.

## REPORT OF A CASE

W. H., a white man aged 42, was admitted to the service of Dr. D. B. Phemister at the Presbyterian Hospital on May 29, 1924. Roentgenograms of the right knee showed a well circumscribed oval area of reduced density involving the upper mesial aspect of the metaphyseal and epiphyseal regions of the tibia. Clinical diagnosis indicated a benign giant cell tumor. At operation the anteromesial aspect of the upper portion of the tibia was exposed through a linear incision, and the lesion was removed for the most part en masse, together with a portion of overlying cortex. The walls of the resulting cavity were then curetted and the wound closed without drainage. During the six months following operation ten roentgen treatments were given. A sinus discharging a serous fluid developed in the wound shortly after operation and persisted for several months, but it finally healed spontaneously.

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From the Department of Surgery of the University of Chicago

1 Herendeen, R. E. Results in Rontgen-Ray Therapy of Giant-Cell Tumors of Bone. *Ann Surg* 23:398 (Jan) 1931

a definite contracture of the adductor, the external rotator and the extensor muscles of the hip. The left hip was dislocated posteriorly, and there was a contracture of the flexor and adductor muscles. The pelvis was tilted upward on the left side. On the right side roentgenograms showed a good acetabulum, with slight changes in the head and neck of the femur, on the left side roentgenograms showed a poor acetabular shelf, with dislocation of the head of the femur posteriorly and changes both in the head and in the neck of the femur (fig 1). A number of unsuccessful attempts were made at reduction of the dislocation by means of skeletal traction. The Roger Anderson type of traction was then applied to correct the pelvic obliquity, and tenotomy of the adductor muscles was performed. This was partly successful, and a Hessing brace was applied with the leg in abduction. The patient lived in another state and has not been heard from since.

CASE 2—M S, a girl aged 10 years, was first seen in September 1933. At the age of 6 weeks she had whooping cough, with a cerebral complication which led to convulsions. At the age of 2½ years a cerebral blood clot was removed, and thereafter the patient made slight improvement. For the past several years the right hip and knee had been flexed and adducted over the opposite leg. About three weeks before she was admitted to the hospital the child suffered one of her periodic "attacks," during which the left leg went into spasm in extension, while the right leg was flexed. Shortly after this the mother noted that the right leg was becoming shorter. Examination disclosed a typical flexion-adduction deformity of the right leg, with dislocation of the hip. Roentgenograms showed a dislocation of the head of the right femur, which was deformed, and a shallow acetabulum with a poor acetabular roof, those of the left hip showed a slight flattening of the head, with a well formed acetabular shelf. An operation was not performed because of the general neurologic condition.

CASE 3—I K, a boy aged 9 years, was admitted to the hospital in December 1933, with a history of spastic triplegia since birth. Tenotomy had been performed elsewhere several times, and the patient came under treatment primarily for the condition of the left hip. The left leg was held in marked adduction, while the right leg was in abduction and external rotation. Roentgenograms showed an apparently normal right hip, with dislocation of the left femur upward and forward. The acetabulum was shallow and irregular in contour, the acetabular shelf was deficient and the pelvis was tilted upward on the left side owing to weakness of the abdominal and spinal muscles. A shelf operation was performed, with transplantation of the tensor fasciae latae muscle, and thereafter turnbuckle casts were applied, with the object of maintaining the reduction. However, as soon as the traction straps were removed the deformity returned, in spite of the fact that an excellent shelf was to be seen. The roentgenogram made by Dr Pomeranz showed that the acetabular shelf projected well beyond the head of the femur and extended down to the region of the great trochanter, encircling the proximal extremity of the femur. The head of the femur appeared to be subluxated slightly upward as compared with the plate made previously. Because of the low grade of mentality and the lack of cooperation, no further operative procedure was deemed advisable, and the patient was transferred to a convalescent home.

CASE 4—F A, a boy, aged 8 years when he was first treated at the hospital in 1928, had been afflicted with poliomyelitis three years previously and had residual paralysis involving the back and both lower extremities. The spinal muscles on the right side were stronger than those on the left. There was a slight flexion deformity at the left hip but no evidence of dislocation. Except for

The patient remained free from symptoms until the spring of 1934, when dull pain, related to physical activity, was experienced in the upper part of the right leg. It gradually became aggravated until March 1, 1935, when the patient was again seen. Physical examination revealed nothing abnormal except in the upper part of the right leg. Here the linear scar appeared healed, there was no erythema of the skin or visible swelling. On palpation there was some tenderness on the mesial side of the tibial tubercle, and the underlying bone felt roughened. The motions of the knee were not impaired. There was no evidence of excess fluid in the knee joint. Roentgenograms of the upper portion of the tibia revealed a rather large oval multiloculated area of reduced density, with irregular longitudinal streaks of increased density and a dense cortex at the lateral margin of the lesion. When the new roentgenograms were compared with those taken eleven years previously, some reduction in the size of the lesion, due to irregular filling in by both dense and cancellous bone, was noted. The mesial cortex also appeared considerably thicker. The clinical diagnosis was either a recurrent benign giant cell tumor or recurrent osteomyelitis at the site of the tumor.

At the second operation, on March 2, 1935, the anterior surface of the upper 3 inches (7.5 cm) of the tibia was exposed through a linear incision, and the periosteum was reflected mesially and laterally. A window  $1\frac{1}{2}$  by 1 inch (3.8 by 2.5 cm) was excised through the cortex, exposing cancellous bone. There was no gross evidence of tumor. The cancellous bone was penetrated laterally, and an oval area filled with fibrous tissue was found and cleaned out. After more cancellous bone was removed mesially, a cavity about  $\frac{1}{2}$  inch (1.3 cm) in diameter was entered and found to contain very spongy bone and fatty and fibrous marrow. The periosteum was then approximated by catgut sutures and the skin sutured with silk. The convalescence was uneventful.

Cultures of some of the tissue removed at operation remained sterile.

*Histologic Examination*—Sections made in 1924 from the tissue then removed and more recent sections made from blocks cut from the preserved material revealed a typical benign giant cell tumor with rather large spindle cell stroma, throughout which were scattered numerous large foreign body giant cells. Some sections from the margins of the lesion, however, revealed nothing suggesting a benign giant cell tumor but showed instead a rather dense fibrous stroma in which were scattered numerous large fat-filled macrophages (foam cells). Such a picture is consistent with what has been described as xanthoma of bone. We have observed such areas in sections of marrow bordering various types of primary and secondary neoplasms in bone, and we feel that the appearance is due to degeneration of the fatty marrow as a result of direct pressure or of tumor infiltration or that it represents a late stage in the resorption of extravasated blood. Thus, sections from all portions of a lesion should be studied before the diagnosis of xanthoma of bone is made.

Sections of the tissue removed from the oval area on March 1, 1935, revealed a dense fibrotic marrow, in which fibroblast nuclei were not numerous. At the margins of this tissue there were coarse trabeculae of cancellous bone. The relation of the latter to the dense fibrotic marrow suggested that the areas of fibrosis were being gradually and very slowly replaced by cancellous bone such as filled the other cavity. The fibrotic areas also exhibited scattered small foci of small foreign body giant cells, with which were a few round cells. These cellular foci were about the border of the fibrous area and probably were associated with the chronic transformative change and did not represent remnants of the giant cell tumor. Such foci did not exhibit active cellular proliferation.

Sections of chips of cancellous bone showed normal fatty marrow and bony trabeculae.

stand Roentgenograms showed a marginal subluxation of the right hip, with bony changes in the pelvis and femur. As a first step in treatment, the contracture of the abduction deformity of the left leg was undertaken, first by means of a plaster bandage and later by stripping the tensor fasciae latae muscle and the gluteus medius muscle from the ilium. Several months later the adduction-flexion deformity of the right hip was overcome by cutting the tensor fasciae latae and the rectus femoris muscles. A shelf was then turned down from the side of the ilium, and the tensor fasciae latae muscle was transplanted to a posterior attachment. Though this made a marked improvement in the patient's condition, the



Fig 2 (case 5) —Roentgenogram showing unilateral paralysis, with a sloping acetabular shelf which was sufficient until trauma led to dislocation. Note the tilting of the pelvis downward on the affected side and the configuration of the head.

result was not considered satisfactory because of the persistence of some pelvic obliquity. This was ultimately relieved in 1934 by means of a plastic operation on the abdominal fascia. Roentgenograms showed the shelf in situ, with correction of the pelvic obliquity. Since his discharge from the hospital, the patient has been walking about with the aid of crutches in a satisfactory manner.

CASE 8—S. T., a girl aged 9 years, was admitted to the hospital in February 1930 with residual paralysis following poliomyelitis of six years' duration. Until one year previously, when she fell, the patient had been able to walk well with

COMMENT

The case described illustrates that although a benign giant cell tumor is clinically controlled for many years, roentgenographic evidence of the lesion may persist. Ingrowth of cancellous bone at the site of the neoplasm may be a very slow process and may require many years for completion. In some instances complete restoration of the normal architecture of the bone may not be accomplished during the life of the patient. Persistence of reduced density in roentgenograms years after curettage does not therefore necessarily indicate persistence or recurrence of the neoplasm. If serial roentgenograms made over a period of months several years after the operation fail to show progression of the lesion and the patient remains free from symptoms, it may be assumed that the lesion is controlled. On the other hand, recurrence of symptoms, even though roentgenographic examination shows no progression of the lesion, justifies reexploration of the site of the tumor.

dislocated, the left leg being higher than the right. Good strength was noted in the adductor muscles. Roentgenograms showed bilateral dislocation of the hips, with no acetabular fossae. A shelf operation was performed on the left hip in May. Roentgenograms made one month later showed a fairly thick and large newly formed acetabular shelf, which extended well beyond the displaced capital epiphysis of the femur. Somewhat later it was noted that the acetabular shelf appeared to have slipped upward and slightly outward. The patient was discharged to a convalescent home in a plaster cast and at the time of writing was reported to be only slightly improved.

CASE 12—L. B., a girl, was afflicted with infantile paralysis at the age of 1 year. She was left with residual bilateral paralysis of the extremities. Treatment before she was admitted to the Hospital for Joint Diseases consisted of the application of a double spica and later the stabilization of the left foot. With the aid

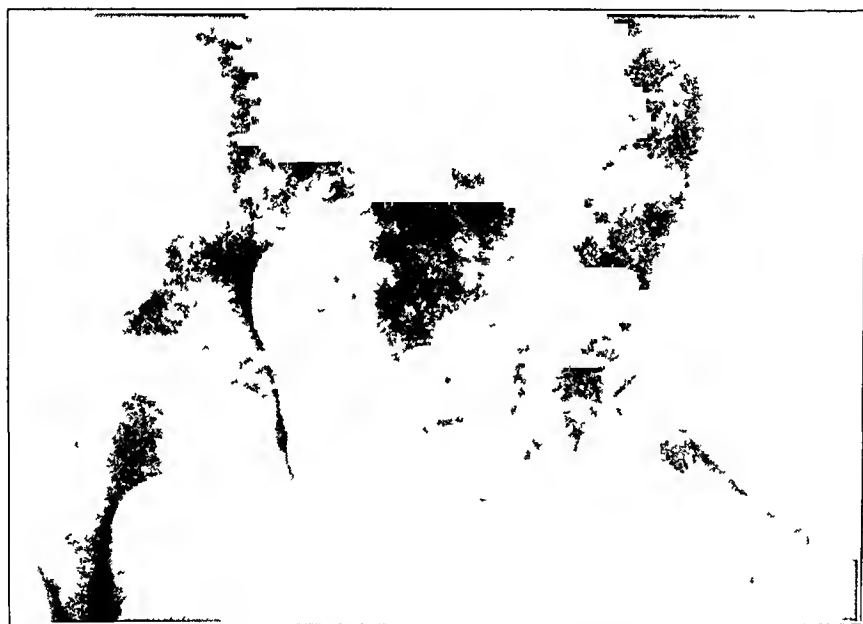


Fig. 3 (case 10)—Roentgenogram showing redislocation of the head despite two shelf operations.

of a brace on the left leg the patient was able to walk. When seen in 1929, at the age of 4, there was a flexion contracture of the left hip with practically no muscle power. The right leg was adducted and flexed. The tensor fasciae latae muscle was strong, and the abductor muscles were weak. Roentgenograms showed that in spite of a fairly good but somewhat sloping shelf there was an upward dislocation of the head of the femur on the right side. The adductor muscles were divided, the hip was reduced and a shelf was turned down superior to the head. The tensor fasciae latae muscle was transplanted posteriorly. The patient was discharged in a plaster cast and was subsequently fitted with a brace. In October 1930, somewhat over a year later, the patient was admitted to the hospital with a recurrence of the flexion of the left hip and dislocation of the right hip. The flexion of the left hip was corrected by means of the Soutter and Yount operations.

tion for the establishment of a bony shelf gave good results. On the other hand Gill<sup>4</sup> in his paper on congenital dislocation of the hip reported nine cases of the paralytic type in only five of which good results followed the shelf operation. Though other authors have reported occasional satisfactory results following one or another procedure it is to be noted that the information on this subject is meager. The consequence of this actual dearth of knowledge is an uncomfortable feeling of uncertainty as to the method best indicated in any particular instance and is the justification for our brief review of the subject.

The series of twenty cases which we have been able to observe in the several orthopedic services of the Hospital for Joint Diseases is admittedly small. Yet the survey of the histories seems to point to certain conclusions which we believe to be of interest and of value.



Fig 1 (case 1) —Roentgenograms showing bilateral flaccid paralysis of the hips with dislocation of the left hip. Note the tilt of the pelvis on the side of the dislocation and also the changes which occurred in the left hip after dislocation and the absence of such changes in the right hip despite the paralysis.

#### REPORT OF CASES

CASE 1—A B, a youth aged 16, was admitted to the hospital in July 1933, about three years after he was shot accidentally. As a result of this he suffered from transverse myelitis. Up to the time of the injury the patient had been well, but within two and one-half years a definite shortening of the left leg was observed. When he was admitted to the hospital bilateral paralysis of the hips was noted. The head of the right femur was in the acetabulum and there was

<sup>4</sup> Gill, A B. *J Bone & Joint Surg* 17:48, 1935. personal communication to the authors.



and abductor muscles and the tensor fasciae latae muscle and to the unopposed action of the sartorius muscle and the adductor muscles. Fusion of the hip was performed, and the patient is still under observation.

CASE 16—N C, a girl, was admitted to the hospital in 1926, at the age of 12 years, suffering from the effects of residual poliomyelitis acquired at the age of 2 years. She had submitted to several operations for stabilization of the ankles. Since our primary interest lies in the hip, the record of the other treatment will be omitted. When the child was 5 years old the mother noted the development of a progressive limp on the right side. When she was first seen, the right hip was flexed and adducted and showed a typical iliac dislocation. The hip was reduced by traction, and a spica was applied and later a brace. The patient was given abduction exercises, but in 1927 roentgenograms showed redislocation, and a shelf operation was performed. In 1929 the patient again showed symptoms, and roentgenograms showed marginal subluxation of the head. In 1934 the patient again returned, complaining of a limp. At this time marked improvement of the abductor muscles was noted, but the head was markedly displaced, and fusion was decided on. The head was pulled down a distance of about 1 inch (2.5 cm) and was fused to the ilium in marked internal rotation. Later, to correct this, supracondylar osteotomy was performed. When seen in the outpatient department about six months later, the patient was walking without the aid of a crutch or brace. There was excellent stability, with a barely perceptible limp. Roentgenograms showed firm bony ankylosis at the hip, with union at the site of the supracondylar osteotomy.

CASE 17—M K, a woman aged 21, was admitted to the hospital in June 1933. As a consequence of poliomyelitis at the age of 2, the patient had residual paralysis of the left leg and dislocation of the left hip. All the muscles of the hip except the sartorius muscle were absent. The left extremity was about 1 inch (2.5 cm) shorter than the right, and there was a definite tilt of the pelvis downward on the left. Roentgenograms showed a dislocation of the hip, with marked underdevelopment of the osseous structures. A combined intra-articular and extra-articular fusion was performed, and the patient left the hospital wearing a plaster bandage. Subsequently the patient suffered a fracture through the fused hip. This was treated by means of Kirschner wires and healed with the leg in slight adduction. Roentgenograms showed bony union at the site of fracture and fusion of the hip. The patient submitted to operation for stabilization of the foot and in June 1934 was discharged walking and in good condition.

CASE 18—P W, a girl, was first treated in 1927, at the age of 8 years, for complete flaccid paralysis of the right upper extremity and both lower extremities and marked paralytic scoliosis following infantile paralysis six years previously. At this time there was no dislocation, and plaster casts and later braces were applied. In 1929 an upward tilting of the pelvis on the left side was observed, and traction was used in an effort to combat the pelvic obliquity. In 1931 the patient was admitted to the hospital for treatment of dislocation of the left hip. The abdominal and the spinal muscles were very weak. The right hip showed a faint trace of muscle power, on the left side the function of the adductor muscles was 2 plus, and the flexor muscles showed a trace of power. The left hip was adducted and the right abducted. Roentgenograms showed dislocation of the left hip. An operation for fusion was performed in December 1931, but the result was not satisfactory. Instead of fusion, there was a wide shelf, which, however, did not function to restore stability of the hip. In November 1932 the hip was refused, and

slight action of the extensor muscle, all the muscles of the right hip were powerless. The same was true of all but the external rotator muscles of the left hip. One ankle was stabilized, and plaster of paris bandages were applied to correct and maintain the correction in the spine and in the extremities. In November 1933 the patient returned to the hospital with a marked flexion contracture of the left hip. The pelvis on the left side was  $3\frac{1}{2}$  inches (9 cm) higher than on the right side and was tilted markedly forward, so that the patient had severe scoliosis and lordosis. Roentgenograms of the right side showed a fairly normal head, neck and acetabulum, while on the left side the head was dislocated, the acetabular roof was poor and the femur was in varus. Because of the debility of the patient and the extent of the paralysis an extensive operation was not considered advisable. The pelvic obliquity was corrected by tenotomy and traction, and the patient was fitted with a brace and a crutch, with which he was able to get about.

CASE 5—H F, a man aged 31, was admitted to the hospital in July 1933. He had poliomyelitis at the age of  $1\frac{1}{2}$  years. At first he was treated by means of a brace, but subsequently he was operated on and was able to get about very well until three years previously, when he slipped. Something "snapped" in his left hip, and since that time he noticed the progressive development of a limp. Examination disclosed a typical dislocation of the left hip posteriorly. The pelvis tended to sink on the left side. The gluteus medius muscle was not present, and the tensor fasciae latae muscle was weak, but otherwise the muscles about the hip were powerful. Roentgenograms showed a sloping acetabular roof and an elongated, widened acetabulum. The head of the femur was well formed but was lying posteriorly, the neck was in valgus and was slightly anteverted (fig 2). An attempt was made to reduce the dislocation by skeletal traction, but the patient refused to tolerate the treatment and left the hospital against advice.

CASE 6—O B, a boy aged 14, was admitted to the hospital on Nov 2, 1929, with a history of infantile paralysis at the age of 6 months. Stabilizing operations were performed on his legs. When he was admitted to the hospital the patient walked fairly well. The left leg was 2 inches (5 cm) shorter than the right leg. There was a flexion contracture of 30 degrees in the left hip. The adductor muscles were more powerful than the abductor muscles, the tensor fasciae latae muscle was good, and the hamstring muscles were somewhat more powerful than the quadriceps muscle. Roentgenograms showed a shallow acetabular cavity with a deficient shelf. The Dickson and Souter operations were performed for flexion contraction on November 20, and a plaster of paris cast was applied. In February 1931 the patient was admitted to the hospital for a bone-lengthening operation, roentgenograms showed the same type of marginal subluxation of the femur, but it was noted that the patient had good stability and so no further operation was performed on the hip.

CASE 7—G J, a boy was first admitted to the hospital in June 1931, at the age of  $6\frac{1}{2}$  years. Poliomyelitis at the age of 8 months left him with paralysis of the right upper extremity and both lower extremities. Examination disclosed a marked upward tilting of the pelvis on the right side, with severe lordosis due to a forward inclination of the pelvis. As was to be expected, the muscles of the spine and abdomen on the right side were much stronger than those on the left side. The function of the abductor muscles of the left hip was 2 plus, that of the adductor muscles of the right hip was 3 plus, and that of the right tensor fasciae latae muscle was 2 plus. The hamstring and flexor muscles of the hip were powerless. There was a flexion contracture of the right hip, which was dislocated. The left hip was flail. Without crutches the patient was unable to

(in one case, as mentioned previously the procedure was done on reoperation) and in two the result was satisfactory after a secondary procedure designed to correct the pelvic obliquity. In the one case in which primary deepening of the acetabulum was attempted the operation was unsuccessful, and an operation for fusion was subsequently performed, with a good result. In seven cases fusion was undertaken. In four of the cases fusion was a primary procedure. The result in one was good, in one refusion was necessary and in two the operation was unsuccessful. In three cases fusion gave a good result after the failure of other surgical measures.

In by far the great majority of cases reported the origin of the condition was poliomyelitic. However, this is not invariably true. Nolut<sup>5</sup> called attention to the fact that paralytic dislocations have been noted in persons with locomotor ataxia and with Pott's disease, with injury to the underlying cord. In our series, in cases 5, 9 and 12 the condition was due to spina bifida, in case 1 it developed following a bullet injury to the cord, with subsequent transverse myelitis, in case 2 there was spasticity in a patient who was obviously suffering from some cerebral disorder, probably hemiplegia following pertussis, and in case 3 the condition was due to a cerebral injury at birth. The latter cases are of unusual interest because dislocation of the hip occurs rarely, if at all, in any of the large group of patients with hemiplegia afflicted with paralysis of cerebral origin. In fact, while dislocations are seldom observed in persons with paralysis which results from lesions of the upper motor neurons, they seem to be typical in persons in whom the lower motor neuron arc is interrupted. The explanation of this remarkable preponderance is undoubtedly to be found in an appreciation of the elements which determine the stability of the hip joint.

Normally this depends on two factors, the character or competence of the acetabular block and the integrity of the pelvotrochanteric musculature. To insure perfect stability, both of these forces must be cooperating, and the loss of either predisposes to instability and dislocation. Of the two, the muscular element is, in our opinion, the more important. This does not in any manner minimize the importance of the acetabular shelf. From the experience gained by surgeons in the treatment of congenital dislocation of the hip, the significance of the shelf has been well attested. It is evident, however, that the data so obtained merely indicate the function of the shelf in the presence of otherwise good muscle power. In cases of paralysis the situation is markedly different, and the application of conclusions reached from the treatment of congenital dislocation to the problem of paralytic

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5 Nolut, T. Contribution a l'etude de la luxation paralytique de la hanche, These de Paris, no 326, 1905, p 7

the aid of a brace. Roentgenograms made at that time showed a dislocation of the left hip, and a plaster of paris bandage was applied. Examination in 1930 revealed a relatively mild form of paralysis. The flexor and extensor muscles of the hip, though reduced in power, were present and were of about equal power. The adductor muscles showed a slight predominance over the abductor muscles, but there appeared to be no definite pelvic tilt and no severe contracture. A typical shelf was turned down from the side of the ilium, and the tensor fasciae latae muscle was transplanted posteriorly in the manner described by Dickson. Roentgenograms showed a large, well formed shelf, with the head lying beneath it. The patient could not be examined recently but is reported to have a good result from the operation.

CASE 9—J. B., a girl aged 5 years, was admitted to the hospital in December 1927 with a history of poliomyelitis two and one-half years previously. The pelvis was inclined forward and definitely upward on the left side. All the muscles of the left hip except the flexor muscles and the tensor fasciae latae muscle were extremely weak. On the right, moderate power was noted in all the muscles except the extensor and adductor muscles. The right leg was held in flexion and abduction contracture, while the left was in flexion and adduction and was dislocated posteriorly. The tensor fasciae latae, the rectus femoris and the psoas muscles and the capsular ligament were contracted, so they were cut. The hip was reduced, and a spica was applied. Roentgenograms showed the reduced hip lying in a poorly formed acetabulum with an insufficient roof. On the right side the head and acetabulum showed only slight abnormalities. After her discharge, the hip was dislocated again, and in February 1928 the patient was admitted to the hospital for tenotomy of the adductor muscle. In 1930 marked lordosis and pelvic obliquity were noted, and the patient was admitted to the hospital for a shelf operation. Roentgenograms showed a well formed shelf with the head in the reduced position. The patient was discharged, walking with the aid of crutches and a brace.

CASE 10—F. B., a girl aged 14 years, was admitted to the hospital in January 1928, with a history of infantile paralysis twelve years before. Only the right leg was involved. The patient had had several previous operations on the ankle with manipulative reduction of the dislocation of the hip. The mother noted that the shortness of the right leg was increasing. When the patient was admitted to the hospital it was noted that there was a definite upward tilting of the pelvis on the right side. The function of the flexor muscles of the hip was 4 plus, that of the gluteus maximus muscle and the abductor muscles of the hip was 2 plus and that of the adductor muscles was 4 plus. There were about 2 inches (5 cm.) of shortening of the right leg, a definite flexion deformity at the right hip of 15 degrees and an adduction deformity of 30 degrees. Roentgenograms showed a dislocation of the right hip. In February 1928 a shelf operation was performed. Roentgenograms made in 1930 showed the pelvis to be somewhat oblique, but the hip was apparently beneath the shelf. In March 1930 the patient was able to walk with the aid of crutches and a brace, which were discarded shortly afterward.

CASE 11—E. R., a girl, was admitted to the hospital in May 1933, at the age of 12 years. At the age of 5 weeks she had been operated on for meningocele and spina bifida. When 1 year old she was able to walk with the aid of crutches. Paralysis of the feet was noted as early as 1926 but the muscles of the hip were considered good. In 1929 it was noted that the child was walking well but that operations for the stabilization of both ankles were indicated. In 1930 it was noted that there was a dislocation of the left hip and in 1931 both hips were

insignificant shelf may be adequate to prevent dislocation. The important factor is the condition of the muscles about the hip. It is our belief that the dislocation of the hip will or will not occur in obedience to the resultant of forces acting on the hip and that the bony changes observed in the head and acetabulum of a dislocated hip are the result and not the cause of the dislocation, as Murk Jansen<sup>6</sup> demonstrated in cases of congenital dislocation.

Karewski,<sup>7</sup> Tillaux<sup>8</sup> and others<sup>9</sup> have demonstrated that when the resultant of forces is such as to lead to flexion, abduction and external rotation of the thigh, there is a tendency toward pubic dislocation. When the thigh assumes the position of flexion and adduction, the tendency is toward iliac dislocation. This is valid, whether the dislocation is of the congenital, traumatic, postinfectious or paralytic variety. The paralytic dislocation is merely a special condition due to the loss of power in some or all of the pelvifemoral muscles. This theory of the mechanism of dislocation by the unopposed action of certain groups of muscles was originally propounded by Reclus<sup>10</sup> and has been generally accepted by those who have given the matter thought. On the other hand, as Riedinger<sup>11</sup> and others have observed, accurate knowledge of the extent of the paralysis is in itself insufficient to warrant prediction of the exact type of dislocation which may be expected in any instance. This is due to the varying association of other factors, such as habitual posture, gravity, weight bearing and trauma. This was pointed out by Bradford,<sup>12</sup> Elzinga and Key<sup>2</sup> and others and was well demonstrated in our case 4. Our patient, though almost completely paralyzed, had a flexion contracture and a dislocation as a result of his position in bed. The condition in case 5, on the other hand, illustrated very well the effects of even minimal trauma in precipitating dislocation in a hip the stabilizing elements of which had been largely reduced by the effects of antecedent poliomyelitis. All of these forces are such as to increase the attitude of flexion and adduction and consequently predispose to dislocation.

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6 Jansen, Murk. *J Bone & Joint Surg* **11** 461, 1929.

7 Karewski, F. *Ann Surg* **10** 226, 1889.

8 Tillaux, P. *J Recherches sur les luxations de hanche*, Paris, Asselin & Houzeau, 1896.

9 Cramer, K. *Arch f Orthop* **9** 26, 1910. A good bibliography is included. Hoyt, W. A. *Ohio State M J* **25** 962, 1929. Silfverskiöld, Nils. *Hemiplegia Spastica Infantilis*, Stockholm, P. A. Norstedt & Soner, 1924. Winterstein. *Deutsche Ztschr f Chir* **242** 357, 1933.

10 Reclus, P. *Rev mens de med et de chir* **2** 176, 1878, *Gaz hebdo de med* **20** 781, 1883.

11 Riedinger, J. *Arch f Orthop* **8** 270, 1910.

12 Bradford, E. H. *Boston M & S J* **108** 73, 1883.

In December 1934 the right hip was operated on again, and an additional shelf was turned down posteriorly, but roentgenograms showed that in spite of an excellent roof marginal luxation of the head had recurred (fig 3)

CASE 13—A L, a girl aged 17, was admitted to the hospital in February 1932, about fifteen years after an attack of poliomyelitis, which left her with residual paralysis involving both extremities. There were marked lordosis and scoliosis. The pelvis was inclined forward and was elevated on the left side. The muscles of the left hip showed fair power of flexion and adduction. All the other muscles were absent. The right hip was completely paralyzed, except that there was slight power in the abductor muscles and good power in the extensor muscles. Roentgenograms showed a well formed head articulating with a good acetabulum on the right side. It was deemed desirable to stabilize the foot before proceeding to the operation on the hip. Several months after this operation, the patient was admitted to the hospital for treatment of the condition of the hip. A shelf operation was performed on the left side in June 1932, though it was realized that the chances for a successful outcome were not good because of the absence of the abductor muscles. This proved to be the case. Four months after the operation the hip was completely dislocated and was unstable, and the shelf was found to have fractured. In December 1932 the patient was admitted to the hospital for a bifurcation operation. Roentgenograms showed firm union at the site of the osteotomy, with reunion of the fragments of the fractured acetabular shelf. When the patient was examined about six months later she was walking with the aid of crutches. The hip was stable in 15 degrees of abduction, and the patient was satisfied with the strength of her leg.

CASE 14—F K, a girl, was first treated in 1926, at the age of 8 years, for severe bilateral paralytic clubfoot and paralytic dislocation of the hip due to spina bifida. The pelvis was tilted upward on the left, and the left leg was consequently in adduction, while the right leg was in slight abduction. There was practically no power in either extremity. Roentgenograms showed dislocation of the left femur, with poor formation of the shelf. The head of the right femur was in the acetabulum, with marked deformity of the neck and a change in the direction of the capital epiphysis. Operations were performed for stabilization of the ankles, and in January 1927 a new acetabulum was reamed out. Though the head seemed to remain in place in all positions of the leg when tested on the operating table roentgenograms made several months later showed a recurrence of the dislocation and an increase in the pelvic obliquity. To correct this the abductor muscles of the right hip and the adductor muscles of the left hip were tenotomized. Thereafter the left hip was fused, and the patient was discharged, walking with the aid of braces and crutches. The patient died about six years later of an intercurrent infection.

CASE 15—F O, a boy aged 7 years, was first admitted to the hospital in June 1934, five years after an attack of poliomyelitis. Only the right leg was involved. The pelvis was tilted downward on the affected side, and there was a moderate increase in its forward inclination. The abdominal and the spinal musculature were normal. The abductor muscles of the right hip were completely paralyzed, and the hip was in definite flexion and adduction contracture. Roentgenograms showed a poorly developed acetabulum, with an inadequate acetabular roof. A shelf was turned down and the tensor fasciae latae muscle was transplanted. Roentgenograms made about six months later showed a recurrence of the upward luxation of the femur. On the patient's admission to the hospital in May 1935 the flexion contracture had become reestablished, owing to the weakness of the gluteal

to its correction, the results seemed to warrant the additional effort. It is possible that neglect in its treatment may account in part for the failures which have been recorded in the treatment of paralytic dislocations.

On viewing the problem of the therapy of paralytic dislocations in the light of the considerations previously noted, it will be seen to be much more complicated than was at first sight apparent. While a mild type offers no insurmountable difficulties, a complicated type may necessitate the solution of several auxiliary problems, each of which may be of major magnitude. The first of these is the question of deformity. To be sure, deformity should be prevented by appropriate application of plaster or a brace, but, willy-nilly, deformities do present themselves and they must be corrected. Not only must the deformity of the hip be corrected, but, of much more importance, the pelvis must be leveled. This may involve complicated surgical maneuvers: traction, application of plaster or a brace, various forms of myotomy or tenotomy, plastic operation on the fascia for paralysis of the abdominal muscles or even spinal fusion. The results may be questionable, yet the neglect of this factor may vitiate adequate treatment of the condition.

Once the pelvis is level, the question of treatment of the condition in the hip itself may be broached. This treatment may be conservative or radical. The conservative measures embrace the use of plaster or of abduction braces. A radical measure may consist of simple myotomy or tenotomy or may involve the performance of a complicated operation. The radical measures may be classified as operations on

- 1 The capsule of the hip joint
  - (a) Reefing or
  - (b) Overlapping, as in the Jones operation
- 2 The bones of the hip joint
  - (a) The acetabulum a shelf operation
  - (b) The neck of the femur Lorenz, Hass or Schanz osteotomy
- 3 The joint
  - (a) Arthrodesis
- 4 The muscles
  - (a) The Dickson operation
  - (b) Transplantation of the gluteal muscles
  - (c) Tenodesis (e g, using the tensor fasciae latae muscle)

In the matter of treatment of the first and third categories, established by Sever, most observers are agreed. In the case of mild involvement without dislocation, treatment should be such as to prevent dislocation. This may be done by elevation of the shoe on the opposite foot, by the application of plaster or a brace or by the performance of myotomy on the affected leg. All these measures are designed to

the patient was discharged to a convalescent home. It was reported that, considering the extent of the paralytic involvement, the patient seems to have shown improvement after the second operation for fusion.

CASE 19—S. L., a girl aged 14 years, was admitted to the hospital in October 1933, ten years after an attack of infantile paralysis. The residual paralysis was mild. The function of the flexor muscles of the left hip was 4 plus, that of the adductor muscles was 4 plus and that of the abductor muscles was 2 plus, function of the extensor muscles was nil. The muscles of the back and abdomen were strong. The leg was held in flexion and adduction, but the pelvis was tilted downward on the left side, the side of the dislocation. This, we believe, is accounted for by the shortening of about  $1\frac{1}{2}$  inch (38 cm.) which existed in the left lower extremity. In January 1935 fusion of the left hip was performed, but the graft did not "take." The further outcome cannot be reported at present, since the patient is to be operated on again.

CASE 20—S. B., a woman, was admitted to the hospital in 1932, at the age of 23. She had apparently been treated for a congenital dislocation of the right hip at the age of 6 years. At the age of 11 years the patient had poliomyelitis, which left residual paralysis in the right hip. On examination the pelvis was found to be tilted upward on the right side, and there was apparently a flexion and adduction contracture. An attempt at fusion of the hip was made without success. Roentgenograms showed a shallow acetabulum, with a poor roof. The head was dislocated, and at the upper end of the shaft there was a peculiar hooklike process, evidently the remnant of the bone graft. The patient is to be admitted to the hospital again for operative fusion.

#### COMMENT

When we analyzed these cases, a number of interesting observations were made. In an active hospital service, a record of only twenty cases could be found over a period of ten years. In the twenty cases there were twenty-one luxations or subluxations of the hip. Though in ten of the cases there was bilateral paralysis of the hip of varying degrees of severity, bilateral dislocation was noted in only one (that of a patient suffering from severe spina bifida). In many cases the tensor fasciae latae muscle possessed considerable power, sufficient so that at operation the muscle warranted transplantation. In its anatomic position this muscle seemed to function more as a flexor than as an abductor muscle of the hip. In practically all cases in which dislocation occurred, the abductor muscles were either absent or so weak as to be valueless as stabilizers of the hip.

In sixteen of the twenty cases, various types of operation were performed. In seven cases the shelf operation alone was performed. Of these, a good result occurred in only two. Of the others, fusion was performed later in two, with good results, an operation for bifurcation gave a good result in one, and in another establishment of an additional shelf and a Dickson operation were employed, with an unsatisfactory outcome. Of the four cases in which the combined shelf and Dickson operations were performed, in two there was a poor result.



# TREATMENT OF GASTROJEJUNOCOLIC FISTULA BY MULTIPLE STAGE OPERATIONS

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## HISTORICAL REVIEW

Gastrojejunocolic fistula is one of the rare complications attending gastric surgical procedure Czerny<sup>1</sup> reported the first case in 1903 Bolton and Trotter in 1920 added four cases to the thirty-four already reported in the literature, while Judd<sup>2</sup> found records of only six cases at the Mayo Clinic previous to 1921 Rankin, Barger and Bue<sup>3</sup> in their book published in 1932 attested to the rarity of the lesion Lahey<sup>4</sup> in 1933 reported the observation of only six cases

Since 1881, when Wolfer introduced the operation of gastroenterostomy, surgeons have had complications following gastric operations Of the late complications following gastroenterostomy, none is more disappointing or more feared by the conscientious surgeon than the development of jejunal ulcer Walton<sup>5</sup> stated "As soon as it is evident that a gastrojejunal ulcer is present, an operation must be performed, for the condition is certain to progress and will give rise to pain, dangerous hemorrhage, or perforation" If the ulcer perforates into the peritoneal cavity, death from spreading peritonitis usually ensues, if the ulcer perforates into the transverse colon distressing diarrhea usually develops, with nausea, fecal vomiting and rapid losses of weight and strength from inability of the patient to obtain adequate nourishment In Paterson's<sup>6</sup> cases the mortality in those in which operations were not performed was 100 per cent

My paper briefly reviews the etiologic factors and the physiologic changes accompanying the lesion and describes the generally accepted methods of treatment A case is reported in detail in which the procedure was successfully carried out in multiple stages, with the Mikulicz procedure

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1 Czerny, Vincenz Beitr z klin Chir **37** 765, 1903

2 Judd, E S Surg, Gynec & Obst **33** 120 (Aug) 1921

3 Rankin, F W, Barger, J A, and Bue, L A The Colon, Rectum and Anus Philadelphia, W B Saunders Company, 1932

4 Lahey, F H S Clin North America **13** 541 (June) 1933

5 Walton, A J, in Nelson Loose-Leaf Living Surgery, New York, Thomas Nelson & Sons, 1928, vol 5, p 154

6 Paterson, H J Internat J Surg **33** 138 (May) 1920

dislocation is fraught with danger unless reservations are made. Thus, in our cases 3, 7, 11, 12, 13, 15 and 18 dislocation occurred in spite of excellent formation of the shelf. On the other hand, the patient in case 5, in whom a sloping shelf was noted, had no difficulty with his hip until the occurrence of a fall. This can be interpreted only as indicating that the stabilizing forces were sufficiently powerful, in spite of the paralysis and the sloping shelf, to prevent dislocation until such time as the additional trauma balanced the scales in favor of the dislocating forces. Elzinga and Key also noted that the size of the shelf or even its character does not seem to determine the stability of the hip. They stated "We believe that an accurate placing of the shelf is more important than its size, as we have found small shelves just as efficient as large ones." Just where the shelf should be placed to be accurate was not stated, and in our opinion the "accurate placing of the shelf" can acquire significance only if by this term is meant the placing of the shelf so that it tends to fortify the stabilizing forces or to oppose the dislocating forces.

Unfortunately, Elzinga and Key did not state in particular the condition of the muscles in those cases in which good surgical results were obtained. They noted, however "In eleven of twenty-six cases dislocation occurred in the presence of definite power in the extensor group. Much the same is true of the external rotators. Apparently the muscles which are most important in lending stability to the hip are the abductors and the tensor fascia femoris, as dislocation occurred in only two cases with fair abductors, in only three cases with a fair tensor fascia femoris and in no case in which these muscles were good or normal." This brings us to a consideration of the second element, the muscle factor, in the stabilization of the hip joint.

Apart from their function in moving the thigh, the pelvitrochanteric muscles act to maintain the contact of the head of the femur against the fulcrum of the acetabulum. When this contact is not maintained, as in the cases in which there is marked effusion into the joint or as in the cases cited here, the dislocation may occur regardless of the normal configuration of the bones. On the other hand, when this contact is maintained, as in cases in which spasticity of the muscles are associated with paralysis of the type caused by involvement of the upper motor neurons dislocation is among the greatest of rarities, though it does occur when the resultant forces are of sufficient magnitude. With paralysis caused by involvement of the lower motor neuron in which the muscles are completely atonic and contact cannot be maintained dislocation will occur (as has been indicated) regardless of the nature of the shelf, while in the less severe cases, in which some muscle power still exists, especially in the extensor or abductor muscles even an apparently

down the intestinal tract Horsley<sup>8</sup> concluded that pathogenic bacteria do not grow in the normal stomach because of the presence of hydrochloric acid and that because hydrochloric acid is not present in the gastric juice of patients with carcinoma of the stomach bacteria do grow For ten years Horsley fed his patients with gastric carcinoma or any other gastric disturbance associated with low acidity dilute hydrochloric acid for several days prior to operation to render the gastric content sterile It is well known that peritonitis from the spill of normal gastric or duodenal contents is rare, while the slightest contamination of the abdominal cavity by the contents of the large intestines results in peritonitis, usually fatal to debilitated patients

#### DISTURBED PHYSIOLOGY

Perforation of a gastrojejunal ulcer into the transverse colon produces certain physiologic changes If the opening into the large intestine is small, very little food passes through it, most of the food taken by mouth being allowed to pass naturally through the entire length of the small intestine Ample opportunity is thus provided for the absorption of nourishment There may be only occasional symptoms referable to the gastro-intestinal tract for some time If there is considerable inflammation or active ulceration about the opening, there may be intermittent periods of bleeding, nausea and vomiting, accompanied by pain and diarrhea If the opening into the colon is large, much of the food passes directly from the stomach and jejunum into the transverse colon and does not have an opportunity to come in contact with the small intestine Large quantities of nourishing food may be eaten but are of no value in supplying nutrition, as there is no opportunity for digestion and absorption by the small intestine Loss of up to 75 pounds (34 Kg) in weight has occurred from the inability of the patient to absorb the food ingested Anemia and extreme weakness rapidly develop

Another disadvantage of the direct opening from the stomach into the colon is the appearance of virulent bacteria in the stomach and upper part of the intestinal tract A normally sterile field is changed into a potentially septic one by the appearance of colon bacilli in the stomach and jejunum These artificial openings, which permit unusual bacteria and alkaline digestive juices to enter the normally acid stomach, frequently cause severe gastritis On the other hand, the sudden appearance of undigested food in the transverse colon often results in the most troublesome diarrhea

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<sup>8</sup> Horsley, J S, in Lewis, Dean Practice of Surgery, Hagerstown, Md, W F Prior Company, 1929, vol 6, chaps 3 and 12

When we speak of flexion and adduction being the dangerous attitude, we mean commonly flexion and adduction of the thigh in relation to the pelvis. But unless we speak of flexion and adduction in respect to a level pelvis, the use of the term is meaningless. It then becomes apparent that if we can draw a conclusion from the attitude of the flexion and adduction of the thigh in relation to the pelvis, we must conclude also that the same ill effects will result from the attitude of forward inclination and upward tilting of the pelvis in relation to the femur. This follows from the fact that flexion of the femur is the equivalent of forward inclination of the pelvis, while upward tilting of the pelvis is the equivalent of adduction of the femur. That these effects may be caused by different groups of muscles complicates the picture but does not alter the fundamental validity of the relationship.

In an excellent paper on the subject of pelvic obliquity, Mayer<sup>13</sup> called attention to the fact that the effective forces in causing a tilting of the pelvis in the lateral plane are (1) contracture of the abdominal and spinal muscles, (2) contracture of the abductor muscles and (3) contracture of the adductor muscles. These three forces, either alone or in effective combination, determine a moment of rotation of the pelvis which results in the five types of lateral pelvic tilting which Mayer described. In a similar manner, tilting of the pelvis in an antero-posterior plane or inclination of the pelvis is controlled by the opposing action of the abdominal and spinal muscles and the flexor and extensor muscles of the thigh. Thus, forward inclination of the pelvis or lordosis may be caused by (1) contracture of the spinal muscles or (2) contracture of the flexor muscles of the thigh and the extensor muscles of the knee.

Except in cases 5, 15, 17 and 19, our patients exhibited a definite upward tilting of the pelvis on the side of the dislocation. In cases 17 and 19 this variation was readily accounted for by the actual shortening of the limb. This tendency to upward tilting is remarkable in view of the fact that in other forms of dislocation the tilting is usually downward on the affected side because of the relative shortening of the limb. Almost all showed, in addition, a marked degree of forward inclination of the pelvis. That this may have been partly due to the posterior dislocation of the fulcrum is immaterial, since the effect of this is merely to increase the efficiency of the forces causing the forward inclination. It leaves unaltered the general conclusion that the pelvic tilting in the anteroposterior and in the lateral plane is due to imbalance of the controlling musculature. Unfortunately, this condition does not seem to have aroused the interest which its importance would seem to merit. In cases 1, 4, 7 and 14, in which special attention was directed

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13 Mayer, L. J. Bone & Joint Surg. **13** 1, 1931

## REPORT OF CASE

*History*—A 58 year old rancher was admitted to the hospital complaining of severe diarrhea of seven weeks' duration, with marked loss of weight and strength. Fifteen years previously a gastro-enterostomy had been performed elsewhere for a duodenal ulcer. Following this operation the patient was free from symptoms for eight years. For the past seven years the patient had noted some gas and burning epigastric distress after eating. This had been partially relieved by baking soda but had never been so severe as to prevent work. Three years previously the patient first noted attacks of diarrhea, occurring chiefly at night. At first these attacks were of from three to four days' duration and occurred at monthly intervals. The attacks gradually increased in frequency and severity. For the preceding two years the patient had been unable to do any work. Seven weeks before he was admitted to the hospital the diarrhea became constant, with from eight to ten stools daily, composed chiefly of mucus and undigested food. Blood had never been noted in the stools, but a marked burning sensation in the rectum had been present. The patient had lost 30 pounds in the past seven weeks and had been confined to the house because of weakness.

The patient's history, except for his gastro-intestinal complaints, was uneventful. He had always been a heavy smoker, but otherwise his habits were not remarkable.

*Physical Examination*—Physical examination revealed the patient to be well developed but poorly nourished, somewhat dehydrated, with evidence of recent loss of weight. Aside from a large right inguinal hernia and the healed scar of the previous laparotomy, the physical findings were normal. The blood pressure was 130 systolic and 80 diastolic.

Laboratory examination revealed normal urine. The stools did not show blood and parasites but did show large quantities of undigested food. The blood picture was that of mild secondary anemia. Gastric analysis revealed marked hyperacidity: free hydrochloric acid 70 and total acidity 80.

*Roentgen Examination*—Fluoroscopic examination by Dr. M. J. Geyman at the Cottage Hospital revealed a somewhat highly placed gastro-enterostomy stoma that appeared to be irregular. Adjacent to the opening a fleck of barium sulfate appeared, suggesting an ulcerated margin. The duodenal bulb was deformed and contracted, but there was no evidence of an active ulcer of the duodenum. Most of the meal appeared to leave the stomach by the gastro-enterostomy opening. In less than thirty minutes barium-coated fecal matter was visible in the rectum and descending colon. After five hours the stomach was empty, and the head of the barium column was in the transverse colon, but it was evident that the sigmoid colon had received the opaque substance from a fistulous tract. A barium sulfate enema confirmed the diagnosis of fistula, the barium going directly from the transverse colon through the fistulous tract into the jejunum. A definite diagnosis of gastrojejuno-colic fistula with possible ulceration was made. The roentgenologist added that he did not believe that sufficient barium left the stomach through the pylorus for the patient to get along without another outlet from the stomach when the fistulous tract was resected.

*Preparation*—Preoperative treatment consisted in emptying the gastro-intestinal tract of barium and in maintaining a normal level of the body fluids and nutrition. As a portion of the intestinal stream was going directly from the jejunum to the transverse colon through the fistulous tract, it was difficult to empty the cecum and ascending colon. Large doses of liquid petrolatum by mouth and repeated

maintain abduction and extension and so to combat the development of the pernicious attitude of flexion and adduction. In the case of severe involvement treatment should be by arthrodesis. We are convinced, with Gill, that in such cases "arthrodesis is the operation of choice" and that when there is complete paralysis of all the muscles of the hip the shelf operation cannot be expected to give a good result. However, not every attempt at arthrodesis is followed by ankylosis of the hip joint, in adults even more than in children this tendency toward failure is pronounced. With this in mind, Sir Robert Jones<sup>14</sup> suggested a procedure which he considered successful. This consisted in relief of the contracture by means of fasciotomy, reduction of the dislocation, plastic fixation of the posterior portion of the capsule and then application of a plaster bandage, with the leg in abduction and extension, over a period of six months. We have had no experience with this method.

It is in the treatment of the condition in Sever's second category, in the cases in which there is reducible dislocation with some residual power, that the greatest divergence of opinion arises. Many authors consider the shelf operation the method of choice, but our own experience does not seem to warrant this feeling of assurance. Though the operations in our series were performed by various surgeons, as to whose skill no question can be raised, the results obtained by the shelf operation, even when combined with the stabilizing effects of the Dickson operation, were far from satisfactory. It is palpably impossible to reconcile such results with those reported by Elzinga and Key except on the basis of a difference in the choice of cases. From the experience gained in case 11, in which the shelf operation was originally opposed on the ground of absence of the gluteal muscles and in which subsequent operation for bifurcation gave a satisfactory result, we may perhaps be permitted to join in Gill's opinion that the shelf operation should be used only when there is evidence of fair power in the gluteal muscles. In other cases the various procedures used in the treatment of congenital dislocation may be attempted with the knowledge that in the event of failure arthrodesis is still held in reserve.

222 West Seventy-Seventh Street

123 West Eighty-Sixth Street

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<sup>14</sup> Jones, Robert, in Jones, R., and Lovett, R. W. Orthopedic Surgery, New York, William Wood & Co., 1923, p. 463

ized tincture of opium to quiet peristalsis. No enemas were given for the twenty-four hours previous to operation because of the danger of carrying fecal content into the stomach. I preferred to rely on the high acidity of the stomach as a bactericidal agent rather than to depend on a more thorough mechanical cleansing. Nothing was given by mouth for twelve hours prior to the operation. The level of the body fluids was maintained by the administration of dextrose intravenously.

Five hours prior to the operation 100 cc. of a concentrate of amniotic fluid was given intraperitoneally.

Preliminary medication consisted of 6 grains (0.39 Gm.) of sodium pentobarbital and  $\frac{1}{4}$  grain (0.016 Gm.) of morphine given in divided doses. The operation was begun with spinal anesthesia, which was adequate for one hour and twenty minutes. The operation was completed with nitrous oxide anesthesia, supplemented with 2 ounces (60 cc.) of ether, which gave excellent relaxation throughout the entire operation.

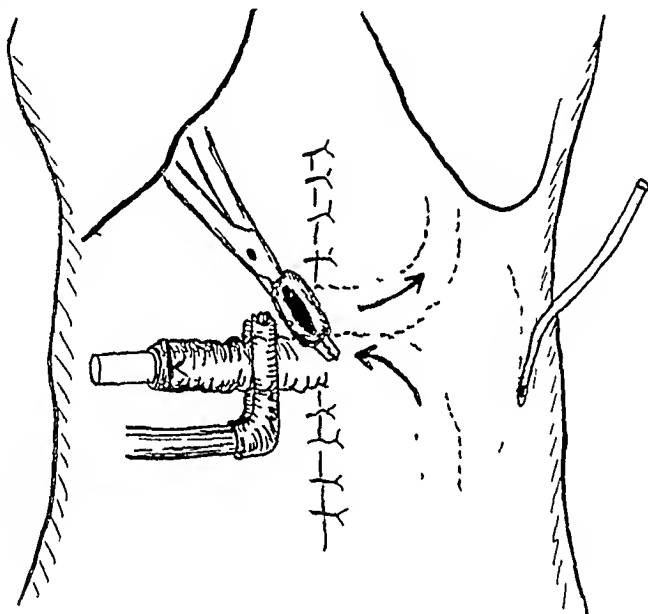


Fig 2—The loop of the transverse colon, with the fistulous tract and the stump of the jejunum, has been removed. The tube is in the proximal limb of the transverse colon for fecal drainage (Lahey method).

*Operation*—When the abdomen was opened the transverse colon and jejunum were found to be adherent over a wide area. The jejunocolic opening was opposite the gastro-enterostomy stoma. The jejunal ulcer apparently had perforated into the transverse colon on the posterior wall near the mesenteric attachment. Both the gastro-enterostomy and the fistulous opening were large and patulous, readily admitting the thumb. There was surprisingly little gross evidence of recent inflammatory reaction around the fistulous tract, although both the jejunum and the transverse colon showed moderate thickening and injection of the vessels of the intestinal wall.

The stomach presented no gross abnormality, and the only evidence of the original ulcer was a fine white scar on the anterior surface of the duodenum, with two constricting bands, one leading to the gallbladder and the other to the liver.

## ETIOLOGY

Many theories have been advanced as to the probable cause of a simple gastrojejunal ulcer. The earlier operators felt that undue trauma to the mucous membrane of the jejunum and faulty technic caused the lesion. Nonabsorbable sutures and clamps were first held responsible for the formation of the new ulcer. Repeated attempts to cure the condition by local excision of the jejunal ulcer resulted in recurrence in over half the cases. The substitution of absorbable cat-gut ligatures for silk sutures failed to prevent the condition. Equally unsatisfactory results followed various forms of gastro-enterostomy. The patients showed marked hyperacidity and a tendency to the formation of ulcers.

## TREATMENT

Until recently the only operation which seemed to give satisfactory results has been partial resection of the stomach, in an attempt to remove a part of the acid-bearing glands. Walton wrote that this operation is one of the most difficult and severe in modern surgery, for not only has the old anastomosis to be freed and separated but the gastrectomy should be extensive, and the ulcerated portion of the jejunum must be removed. The resultant mortality has been very high, ranging from 10 to 40 per cent, with recurrence in over half the surviving patients. With recent studies showing that the gastric glands near the pylorus produce an alkaline rather than an acid secretion, it is evident that a large part of the central portion of the stomach must be removed to lower the acidity to an appreciable degree. During the past decade gastro-enterologists have made distinct advances with diet and chemotherapy. Since they can now accurately control the levels of gastric acidity, it is seldom that an extensive gastric resection, with its attendant dangers, is warranted solely to control acidity.

When the gastrojejunal ulcer is complicated by a fistulous tract leading to the colon, the surgical work is increased, and the dangers of peritonitis from fecal contamination are very great. It is no wonder that such an experienced operator as Lahey wrote "I approach gastrojejunal ulcer with colonic fistula still with hesitation and fear as to the question of possible fatality."

## PHYSIOLOGY

Harvey Cushing<sup>7</sup> demonstrated many years ago that the gastric and duodenal contents were relatively sterile in normal persons and that bacteria increased in numbers and virulence as one progressed

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<sup>7</sup> Cushing, Harvey, in Howell, W. H. *Textbook of Physiology*, ed. 11 Philadelphia, W. B. Saunders Company, 1930.



the transverse colon with questionable circulation was brought outside the peritoneal cavity through the middle of the abdominal incision, according to the method of Mikulicz, and the abdomen was closed

*Postoperative Course*—The postoperative convalescence was very satisfactory. The body fluids and nutrition were maintained at a normal level by the intravenous administration of dextrose for thirty-six hours after the operation. At that time liquids in small amounts were given by mouth, supplemented by feedings through the jejunostomy tube. There was no vomiting, and additions were gradually made to the diet. On the eleventh postoperative day the jejunostomy tube was removed, and the opening closed spontaneously.

Much to my surprise the patient began to pass flatus by rectum on the second postoperative day, and fecal movement began on the fifth day, so that it was

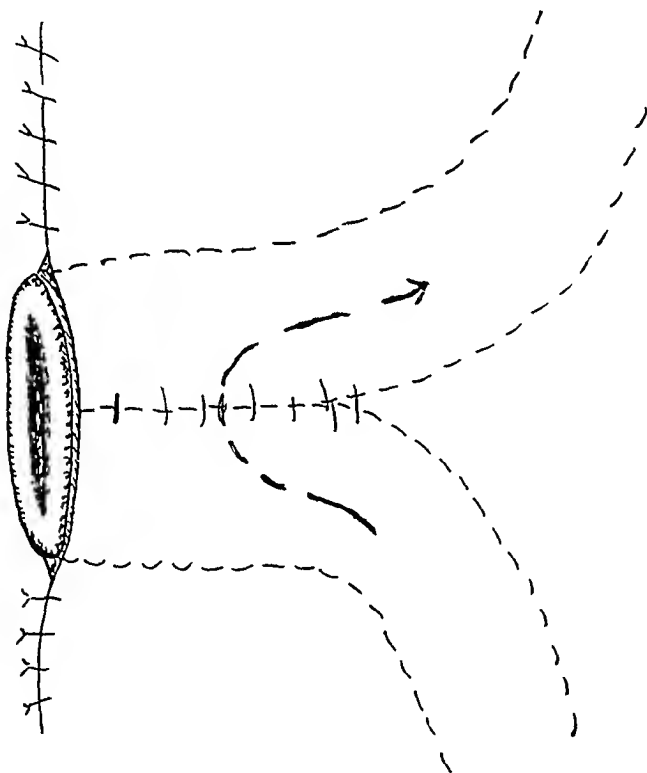


Fig 4—The spur is removed, and the fecal stream is restored. Extraperitoneal closure of the colostomy opening can now be performed to complete the procedure by various methods.

unnecessary to open the colostomy stoma for two weeks. At that time the segment of bowel with the constricted lumen was removed with the cautery. The crushing clamp was applied to necrose the septum between the two limbs of the transverse colon. Five days later the clamp came away, and after this most of the fecal stream was passed by rectum. Aside from a superficial infection in the fascia of the abdominal wall, the patient had no complications and was able to leave the hospital on the twentieth postoperative day. He returned three weeks later and closure of the temporary colostomy opening was then done.

## SURGICAL RISK

Gastrojejunocolic fistula combines the hazards present in gastric operation with all the risks involved in surgical procedures on the colon. Usually the patient is dehydrated, emaciated and anemic. Surgical shock, hemorrhage, peritonitis and infections of the respiratory tract are the chief enemies. Every possible effort should be made to reduce these hazards. Prolonged operations, hours of general anesthesia and excessive handling of the viscera must be avoided. Scrupulous and exacting attention must be given to every detail of technic. The intravenous administration of dextrose, transfusions of blood and the ingestion of large quantities of carbohydrate in the form of fruit juices will frequently change the dehydrated, undernourished, anemic patient into a fair surgical risk.

## PERITONEAL IMMUNIZATION

A preliminary injection of a concentrate of amniotic fluid advocated by Young,<sup>9</sup> is a simple, rapid, nonhazardous and effective method of increasing peritoneal resistance. This procedure promises to supplant the more troublesome, painful and time-consuming method of introducing colon bacilli and streptococci as an intraperitoneal vaccine, with which Rankin and Barger so ably pioneered. I have injected amniotic fluid many times without the slightest discomfort to the patient. Rarely, the fluid spreading throughout the general peritoneal cavity has caused slight nausea, but many times the patient has not been fully aroused from sleep by the procedure. Within a few hours there is usually a rise in temperature of 1 or 2 F° accompanied by a leukocyte count from 15,000 to 20,000 and an increase in the leukocytic content of the peritoneal exudate, which becomes turbid. This increase in the activity of the peritoneal exudate is held by Young<sup>10</sup> and Johnston to be direct evidence of the effectiveness of the immunization.

## NEW APPLICATION OF THE MIKULICZ PROCEDURE

Recently I have used the following method of dealing with gastrojejunocolic fistula with satisfactory results. The method is reported in the hope that it may be of help to others faced with a similar problem. While doubtless other surgeons have employed multiple stage operations for this distressing condition, no report has been found in the literature of utilization of the Mikulicz procedure in this type of case. Extraperitoneal resection of the large intestine has increased the margin of safety in surgical intervention in cases of malignant disease of the colon. Application of the same principle should lower the mortality in cases of gastrojejunocolic fistula.

<sup>9</sup> Young, E. L., and Marks, G. *Surg., Gynec. & Obst.* 59:610 (Oct.) 1934.

<sup>10</sup> Young, E. L. Personal communication to the author.

sive block dissection if any attempt is made to treat the lesion radically. The Mikulicz procedure should be of value here as well as in cases of gastrojejunocolic fistula.

#### SUMMARY

A brief review of the etiology, altered physiology and present methods of dealing with gastrojejunal ulcer and its complications is given.

A case of gastrojejunocolic fistula with successful treatment by graded operation is reported.

The additional safety factors of preoperative peritoneal immunization, simplified multiple stage operations and the use of the Mikulicz procedure are stressed.

enemas partially emptied the large intestine, but considerable barium still remained at the time of operation. Because of diarrhea it was deemed inadvisable to attempt a long period of preparation. The patient was given large quantities of fruit juices for only twenty-four hours before the operation, accompanied by a deodor-

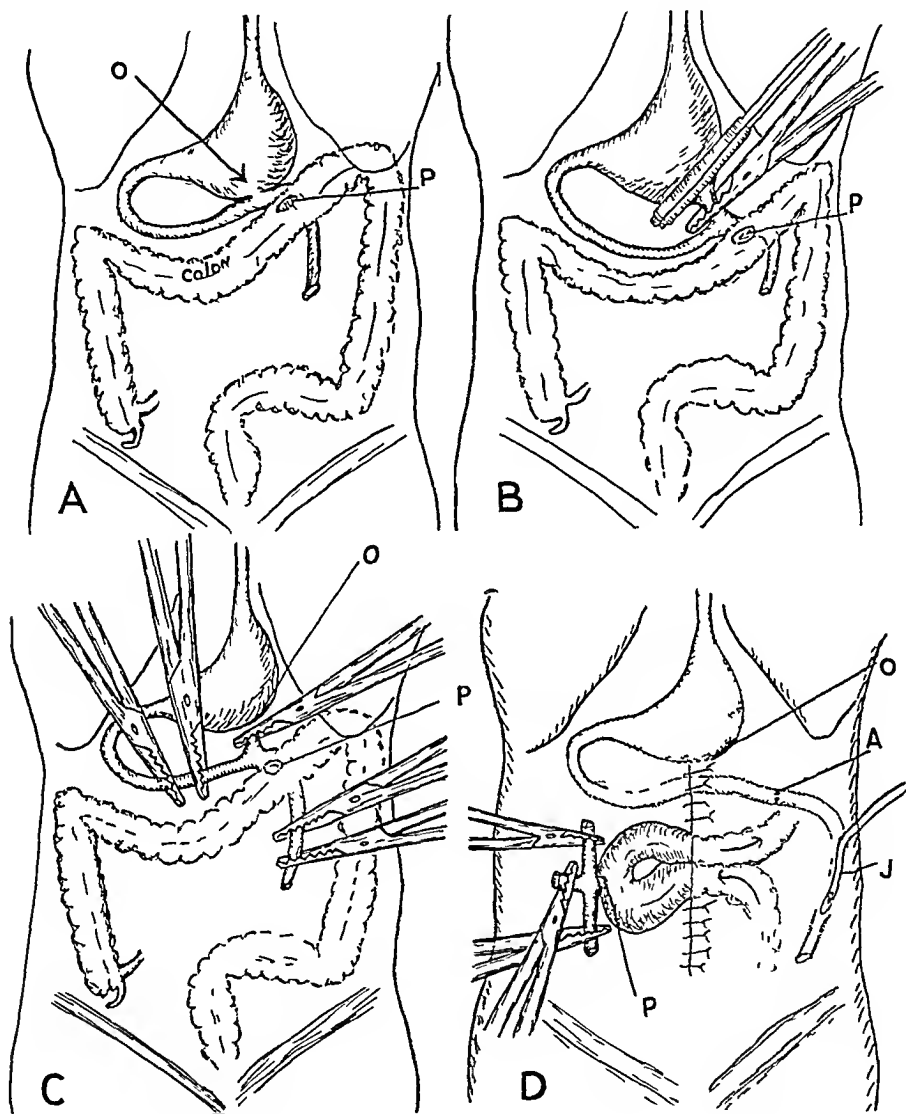


Fig 1—In *A* the jejunal ulcer had perforated into the transverse colon on the posterior wall near the mesenteric attachment. *P* indicates the colonic fistula, and *O*, the gastro-enterostomy opening. In *B* the clamps are applied for resection of the gastro-enterostomy. *P* indicates the colonic fistula. In *C* the gastro-enterostomy is separated, and the opening into the stomach is closed. The clamps are in place for resection of the jejunum. *O* indicates the previous opening in the stomach, and *P* the colonic fistula. In *D*, jejunal anastomosis (*A*), completed, with the catheter (*J*) in place for feeding. The loop of transverse colon with the stump of jejunum attached is brought outside of the abdomen for the Mikulicz drain. *P* indicates the colonic fistula.

## OBSERVATIONS

*Symptoms on Admission*—The most common symptom on the patient's admission to the hospital was shock, with its attending signs, such as pallor, cold, clammy skin, restlessness, rapid, thready pulse, subnormal temperature, thirst and, at times, vomiting. The degree of shock varied roughly in direct proportion to the extent or the seriousness of the trauma and in the majority of the cases indicated the extent of coexisting hemorrhage. In 73 per cent of the cases signs of shock were present or reappeared after treatment and continued until death.

The degree of pain and its distribution depended on the extent and the character of the injury. In a few cases of clean stab wounds the pain was so slight that the patient walked to the hospital. The extensive or macerating injury produced the most pain.

None of our patients showed bradycardia, as described by McKnight<sup>1</sup> and by Erdely,<sup>2</sup> but when this symptom is present, one must not underestimate the degree of hemorrhage.

*Blood Counts on Admission*—Laboratory evidence of anemia and intra-abdominal injury was present at the time of admission in the twenty-four cases in which complete blood counts were made. In all but two of these cases there were severe intra-abdominal hemorrhages.

The hemoglobin content (Dare) varied from 40 to 90 per cent and in one half of the cases it was below 70 per cent. The red cell count varied from 2,800,000 to 5,500,000. In 77 per cent of the cases the count was below 4,000,000. The white cell count varied from normal to 33,000, and in 62 per cent of the cases it was above 10,000. The polymorphonuclear count varied more constantly than any other finding and ranged from a normal value to 90 per cent. In 91 per cent of the cases the count was over 70 per cent, and in 71 per cent it was over 80 per cent. Complete blood counts, and especially the red cell count and the hemoglobin content, are valuable aids in differentiating hemorrhagic shock and traumatic shock, they are of still greater value when determinations are repeated at regular intervals for comparison.

*Operation*—Fifty-five patients were operated on, five were treated medically. Operation was performed promptly after adequate response to the treatment for shock and hemorrhage.

Ether was used in forty-four cases, spinal analgesia, in twelve cases. In view of a previous survey<sup>3</sup> on the use of spinal analgesia in emer-

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1 McKnight, R. B. Post-Operative Physiological Studies in a Case of Traumatic Liver Rupture, *Am J Surg* 8:542 (March) 1930.

2 Erdely, J. Recovery from Multiple Ruptures of the Liver with Intestinal Injury. Diagnosis and Treatment of Subcutaneous Rupture of the Liver, *Deutsche Ztschr f Chir* 198:110, 1926.

3 Krieg, E. G. Spinal Anaesthesia in Cases of Emergency Surgery, *J Michigan M Soc* 31:456 (July) 1932.

After these bands were freed the index finger could readily be passed through the pyloric ring and through the first portion of the duodenum

With some difficulty the adhesions between the stomach, the jejunum and the transverse colon were separated and the fistulous tract was isolated. The gastro-enterostomy anastomosis was first severed between clamps, and the opening into the stomach was closed longitudinally without resulting deformity. The jejunum was then divided between clamps placed on each side of the fistulous tract, about 5 inches (13 cm) of the jejunum being excised. The stump of jejunum, with the fistulous tract leading into the transverse colon, was removed with a wide margin of large intestine. Aseptic closure of the opening into the transverse colon was accomplished.

The severed ends of the jejunum were then united by end-to-end suture. Ten inches (25 cm) distal to the anastomosis of the small intestine a jejunostomy was

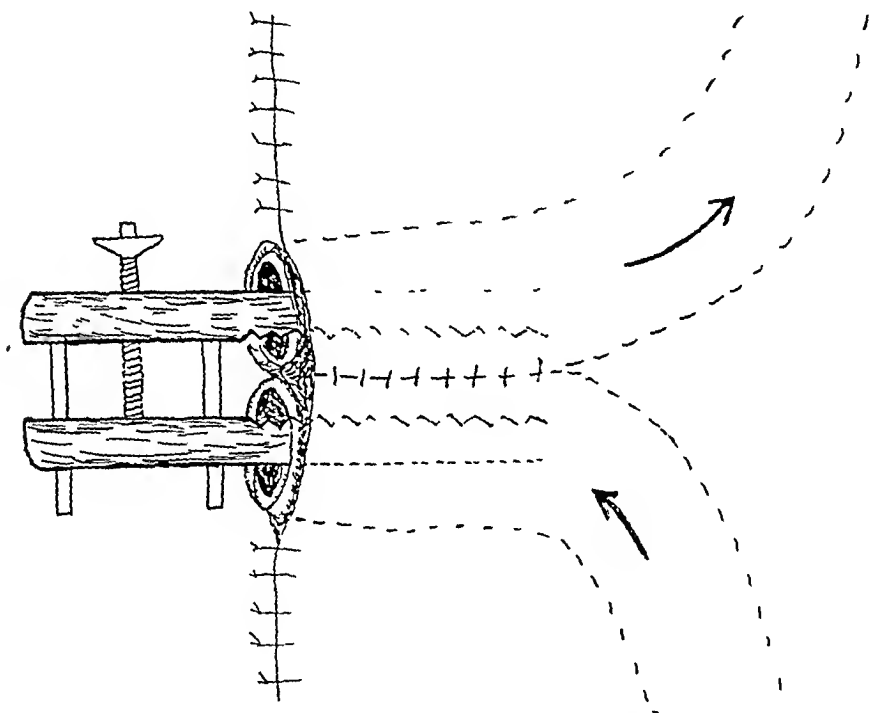


Fig 3—The clamp is in place for removal of the septum by pressure necrosis. Note the special teeth on the clamp.

performed by the Witzel method, using a no 16 double-eyed catheter, which was brought out through a stab wound in the left upper quadrant of the abdomen. This provided a means of feeding the patient until the jejunal anastomosis had healed and would serve for a longer period as well if the duodenum should prove to be as constricted as the roentgenologist had reported. The openings in the mesentery of the transverse colon and into the lesser omental cavity were then closed. To my disappointment, examination then revealed that suture of the transverse colon following excision of the fistulous tract had resulted in marked narrowing of the lumen, with some evidence of impaired circulation in the wall of the bowel. At this time the anesthetist reported that the patient's pulse was slightly irregular, and as nearly three hours had elapsed since the operation had been started, it seemed imperative to finish quickly. Therefore, the narrow portion of

Another patient, who had been struck by an automobile, was in poor condition for four days and then gradually improved. All signs of intra-abdominal hemorrhage were present, including a fluid wave in the abdomen. The hemoglobin content was 40 per cent, and there were 2,950,000 red blood cells. He was discharged on the twenty-third day.

The third patient, who had been run over by an automobile, improved under treatment for a week. On the eighth day restlessness and abdominal pain began, and they continued for four days. On the tenth day abdominal distention began, continuing until death, and the pulse rate, which had ranged within normal limits, began to rise slowly. The patient became irrational on the fifteenth day, and vomiting began on the seventeenth day. Death occurred nineteen days after the accident.

At autopsy the liver revealed a large healed laceration, with fibrosis in the right lobe near the gallbladder. The gallbladder was ruptured, and the abdomen was filled with bile.

*Progress After Primary Shock or Operation*—In all the patients who survived the effect of shock and hemorrhage the condition progressed in one of two ways. The recovery of the first group was comparable to that of any other group of patients on whom laparotomy has been done for a "clean" condition. In the second group certain symptoms developed, and there were complications which were attributed to the pathologic condition of the liver. In this group there were thirty-one patients.

Irrationality or stupor was noted in thirteen cases. This symptom was more frequently intermittent but at times it was continuous, it was noted mostly at night. Extreme irritability was noted in seven cases. The characteristics of this symptom paralleled those of irrationality. It is probable that this symptom is only a stage of irrationality. Vomiting was present in eleven cases and suggested that found when the stomach is dilated or obstructed. Jaundice was present in one patient, it appeared in the first twenty-four hours.

The onset of these symptoms was more frequent during the first three days and especially on the second day. None of our patients survived in whom any one of these symptoms persisted for two days or longer. None lived when any combination of these symptoms appeared. The mortality of the combined group of patients exhibiting the first two symptoms was 85 per cent. The total mortality for the entire group was 74 per cent (tables 3 and 4).

The pulse rate averaged about 90 per minute, and the average temperature was about 99 F, except for the postoperative and the preagonal rise. These observations certainly point to a toxic condition on a noninfective basis.

The third of the patients treated without operation whose cases have been described had all the symptoms and findings under discussion, and his case supports the contention that the condition was toxic without infection.

At the time of writing the patient's gastric acidity is well controlled by medical measures, and fluoroscopic examination shows no signs of duodenal obstruction or irritation. There are no indications for further surgical intervention. A check-up will be made six months later.<sup>10a</sup>

#### COMMENT

Walters,<sup>11</sup> of the Mayo Clinic, reported a case of gastrojejunocolic fistula in a debilitated patient with pyloric obstruction on whom he planned to operate in two stages. At the first operation Walters eliminated the gastroenterostomy anastomosis and closed the colonic fistula, performing a jejunostomy to have a means of feeding the patient between operations. Although in his case the roentgenologist had reported no barium leaving the pylorus previous to operation, food passed freely from the stomach immediately after the first operation, and the jejunostomy tube and second operation were never needed. A check-up six months later showed the patient to be in excellent health, symptom-free and with no clinical or roentgenologic evidence of reactivation of his old duodenal ulcer.

Careful search of the literature fails to reveal a previous report of the use of the Mikulicz procedure in cases of this condition. Its advantages in the prevention of peritonitis have been established. Since 60 per cent of the reported deaths in cases of gastrojejunocolic fistula are due to peritonitis, the Mikulicz procedure should be utilized. I am convinced that faced with a similar problem again, I should carry out the Mikulicz procedure immediately after dividing the jejunum and not attempt to excise the fistulous tract at the time of operation. To attempt excision of the fistula and closure of the colon prolongs the operation and needlessly increases the danger of peritonitis. The colonic fistulas in these cases are often so close to the mesentery and so large that any form of suture is likely to result in narrowing of the lumen or impairment of the blood supply.

Involvement of the mesentery of the transverse colon is often observed in cases of carcinoma of the stomach, which requires exten-

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10a The patient gained 40 pounds (18 Kg) in three months. He returned six months after the operation for fascia lata repair of the inguinal hernia. At that time he was free from symptoms, and the gastric analysis showed free hydrochloric acid 46 and total acid 58. The patient was able to do his usual work as a rancher. A roentgenogram made one year after the operation failed to show any evidence of duodenal ulcer, the stomach was entirely empty of barium sulfate in two hours. The patient's acidity is controlled by frequent feedings and by the omission of tobacco. Gastric analysis showed free hydrochloric acid 50 and total acid 60, one year after the operation.

11 Walters, Waltman, and Priestley, J. T. Proc. Staff Meet., Mayo Clin 8:33 (Jan 18), 339 (May 31) 1933.



in which an automobile accident caused rupture of the gallbladder. The spleen was involved in more cases than was any other organ, and damage to it was always associated with injury to the left lobe of the liver. The mortality in this group was 94 per cent (table 7).

*Hemorrhage*—Abdominal hemorrhage was found in every case and varied in degree, depending on the extent of the injury. The extent and the severity of the injury coincided in the majority of cases. Hem-

TABLE 6—Data on Forty-One Cases of Hepatic Damage Only

Degree of Injury	Stab				Trauma				Clean Bullet Wound				Macerating Bullet Wound			
	Right Lobe		Left Lobe		Right Lobe		Left Lobe		Right Lobe		Left Lobe		Right Lobe		Left Lobe	
	L	D	L	D	L	D	L	D	L	D	L	D	L	D	L	D
	2	3	4	0	1	6	2	0	1	3	2	1	4	4	1	0
Deep																
Superficial									3	0			4	0		

TABLE 7—Other Organs Than Liver Involved, Twenty-One Cases

	Right Lobe	Left Lobe	Both Lobes	Total	Recovery	Death
Spleen	0	4	0	4	0	4
Stomach	2	3	1	6	0	6
Small bowel	2	1	0	3	1	2
Diaphragm	3	1	0	4	0	4
Colon	1	1	0	2	0	2
Spinal section	1	0	0	1	0	1
Gallbladder	1	0	0	1	0	1
Total	10	10	1	21	1	20

TABLE 8—Mortality in Relation to the Degree of Abdominal Hemorrhage

Degree of Hemorrhage	Death	Recovery
Slight	0	2
Moderate	2	7
Severe	35	14

orrhage was classified as slight, moderate and severe. Tables 8 and 9 show interesting findings.

The more recent conception of the mechanism of shock produced by hemorrhage and its treatment has been clearly described by Freeman,<sup>10</sup> in a recent paper. Loss of large amounts of blood causes a powerful stimulation of the adrenal glands to produce epinephrine, in an effort to keep up an adequate circulation of fluid by constriction of the peripheral

10 Freeman, N. E. Hemorrhage in Relation to Shock, *Ann Surg* 101: 484 (Jan) 1935.

# HEPATIC TRAUMA

## ANALYSIS OF SIXTY CASES

EARL G KRIEG, M D

DETROIT

This paper is a survey of the cases of sixty patients who had undergone hepatic trauma who were brought to the City of Detroit Receiving Hospital during the period from 1927 to 1934, inclusive, and represents with some degree of accuracy the frequency of this condition in Detroit. Practically all patients with a condition of this nature are brought into the emergency ward by police ambulance a short time after the accident.

The distribution of the patients in regard to age, color and sex is shown in table 1. The majority were in the so-called age period of greatest activity.

TABLE 1—*Age, Color and Sex Distribution of Patients*

Age Years						Color and Sex			
						Negro		White	
3 to 4	10 to 20	20 to 30	30 to 40	40 to 50	Over 50	Male	Female	Male	Female
2	9	29	10	7	3	21	4	31	4

TABLE 2—*Mode of Injury*

Gunshot (41)										Trauma (10)				Stab (9)			
Quarrel		Police		Robbery		Accident		Suicide		Unclassified		Auto-mobile		Fall			
Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
9	7	6	0	6	0	5	0	1	0	8	0	7	2	1	0	7	2

Injury to the liver in every case in this series was caused by external violence. The patients were divided into three groups: those with gunshot wounds, 68 per cent, those with trauma, such as that caused by an automobile, a street-car or a fall, 17 per cent, and those with stab wounds, 15 per cent. The largest subgroup in any of these divisions was made up of persons taking part in the eternal triangle, and, as one can surmise, about 50 per cent of the patients were women (table 2).

## SUMMARY

The mortality for the whole group was 61.6 per cent, the mortality in the group in which operation was performed was 56.6 per cent. The most serious prognosis obtains in cases of contusion (caused by automobile accident, etc.), deep wounds or injury to the right lobe of the liver and in those in which contiguous organs are also involved.

Irrationality, irritability, vomiting and jaundice are serious prognostic signs.

Hemorrhage was always present, extensively in 80 per cent of the cases. Immediate adequate replacement of fluid is indicated, epinephrine should not be given.

Deep hepatic wounds are best treated by small drains inserted deeply, suture is adequate for superficial wounds, abdominal drainage is necessary in all cases.

Shock due to trauma and hemorrhage caused 73 per cent of the patients in whom they occurred to die within seventy-two hours. Bile peritonitis was the next most frequent cause of death.

1842 David Whitney Building

gency cases, I do not believe that it should be used in the presence of severe hemorrhage such as one finds in cases of hepatic trauma

The hepatic wound was treated by packing in forty-one cases and by suture in fifteen cases. It is of interest to note that in the majority of cases the gauze was not inserted into the wound with enough pressure to control hemorrhage and frequently it was merely placed against the wound, yet in no case was there alarming bleeding after the patient returned to the ward. In several of the cases large amounts of gauze were packed into an area of extensive trauma, and in all these there developed symptoms of obstruction. Dragstedt<sup>4</sup> has shown in dogs that even a minor degree of pressure in this region easily produces obstruction. Walters<sup>5</sup> has shown experimentally and clinically that a definite syndrome is set up by pressure about the liver.

The experiences of Anderson,<sup>6</sup> Halstead,<sup>7</sup> Robertson and R. R. Graham,<sup>8</sup> A. J. Graham<sup>9</sup> and Tilton<sup>9a</sup> suggest that the insertion of a small pack or drain into the deep hepatic wounds is the method of choice. Drainage is imperative for deep hepatic wounds, to prevent encapsulated collections of blood, bile and pus. Suture of the clean superficial wound is adequate. Leakage of bile in some degree is present in all cases, and it would appear that abdominal drainage of some type is necessary regardless of the technic used.

*Treatment Without Operation*—Of the five patients treated medically, two died within three hours. The other three were children in an extreme state of shock, and improvement was not shown until after the third day.

One patient had a gunshot wound through the dome of the liver and the diaphragm, and signs of subdiaphragmatic abscess developed six weeks later. Transpleural drainage was done, but no pus was obtained. The wound drained for several days and healed promptly. The patient was discharged two weeks later. It is most probable that her condition was similar to that in the cases described by Robertson and Graham,<sup>8</sup> Graham<sup>9</sup> and Anderson,<sup>6</sup> in which a collection of blood or bile was present in the substance of the liver.

4 Dragstedt, C. C. Acute Dilatation of Stomach, *J. A. M. A.* **79** 612 (Aug. 19) 1922.

5 Walters, W. Accumulated Bile Displacing Liver, *Surg., Gynec. & Obst.* **47** 421, 1928.

6 Anderson, L. Central Ruptures of Liver and Their Complications, *Beitr. z. klin. Chir.* **135** 696, 1926.

7 Halstead, A. E. Four Cases Requiring Liver Surgery, *S. Clin. North America* **3** 973 (Aug.) 1923.

8 Robertson, D. E., and Graham, R. R. Rupture of Liver Without Tear of the Capsule, *Ann. Surg.* **98** 899 (Nov.) 1933.

9 Graham, A. J. Subcutaneous Rupture of the Liver, *Ann. Surg.* **86** 51 (July) 1927.

9a Tilton, B. J. Considerations Regarding Wounds of Liver, *Ann. Surg.* **9** 27 (Jan.) 1905.

crystalline molecular arrangement which is recordable on photographic film. The principle is the same as the diffraction grating, in which a series of finely drawn black lines on plate glass interfere with rays of visible light, causing them to be broken up into a spectrum.

De Jong<sup>2</sup> found in all specimens of bone examined, both ancient and modern, lines typical of the apatite group of calcium phosphate minerals, this means that calcium phosphate [ $\text{Ca}_3(\text{PO}_4)_2$ ] and calcium carbonate [ $\text{CaCO}_3$ ] are present as a double salt rather than as mixtures of calcium phosphate [ $\text{Ca}_3(\text{PO}_4)_2$ ] and calcium carbonate [ $\text{CaCO}_3$ ]. This work was confirmed<sup>3</sup> and extended by Roseberry, Hastings and Morse,<sup>4</sup> who found that most of the lines in both bone and teeth corresponded closely with the apatite mineral dahllite and that calcium carbonate [ $\text{CaCO}_3$ ] does not exist in bone as such. J. H. Clark<sup>5</sup> showed that the apatite crystals in the shaft of a long bone have a tendency to longitudinal orientation, and she presented evidence that organic crystals (collagen) are present. G. L. Clark and Mrgudich<sup>6</sup> confirmed J. H. Clark's observation regarding the orientation of inorganic crystals along the surface of the long axis of the humerus of the rat and found that this tendency to long fiber orientation was not normally present in regions of bone where tendons or bony processes were attached or during the active and healed stages of rickets.

This idea that the inorganic salts of teeth and bone are similar to the apatite salts of nature is not new but was postulated by Hoppe<sup>7</sup> in 1862 on analytic grounds. Further evidence<sup>8</sup> obtained by stoichiometric methods supports this view. The formula for the inorganic salts of bone proposed by de Jong gives the most reasonable concept of the normal inorganic crystallites  $3\text{Ca}_3(\text{PO}_4)_2 \cdot \text{CaX}_2$  in which  $\text{X}_2$  represents  $\text{CO}_3$ ,  $\text{O}$ ,  $\text{Cl}_2$ ,  $\text{F}_2$ ,  $(\text{OH})_2$ ,  $\text{SO}_4$ .

This formula may be regarded as adequately explaining the normal bone salts, but it does not indicate the quantitative amounts of the various apatite salts present which apparently depend on other factors. Morgulis<sup>9</sup> made a significant observation that in the bones of marine fishes the calcium phosphate [ $\text{Ca}_3(\text{PO}_4)_2$ ]-calcium carbonate [ $\text{CaCO}_3$ ] ratio is radically different from that in all other animals examined, and he logically accounted for the diminished amount of calcium car-

2 de Jong, W. F. *Rec. d. trav. chim. d. Pays-Bas* **45** 445, 1926.

3 Taylor, N. W., and Sheard, C. *J. Biol. Chem.* **81** 479, 1929.

4 Roseberry, H. H., Hastings, A. B., and Morse, J. K. *J. Biol. Chem.* **90** 395, 1931.

5 Clark, J. H. *Am. J. Physiol.* **98** 328, 1931.

6 Clark, G. L., and Mrgudich, J. N. *Am. J. Physiol.* **108** 74, 1934.

7 Hoppe, F. *Virchows Arch. f. path. Anat.* **24** 13, 1862.

8 Gassmann, T. *Ztschr. f. physiol. Chem.* **70** 161, 1910. Bogert, L. J., and Hastings, A. B. *J. Biol. Chem.* **94** 473, 1931.

9 Morgulis, S. *J. Biol. Chem.* **93** 455, 1931.

Bronchitis was present in six cases, but all the patients recovered rapidly. Abdominal distention requiring active treatment occurred in five cases, one of which was an instance of infective peritonitis following secondary closure.

*Hepatic Wounds*—Hepatic wounds are divided generally into deep and superficial wounds. Four types are further described in this survey, as follows: (1) clean incision produced by a stab, (2) clean puncture by a bullet, (3) macerating puncture by a bullet and (4) rough fracture caused by contusion.

TABLE 3—*Onset of Symptoms (in Days)*

	1	2	3	4	6	8	9	14	15	19	Total
1 Irrationality	2	5	2		1		1	1			13
2 Irritability	1	4	1			1				1	7
3 Vomiting	1	4	2	1	1	1			1	1	11
Total	4	13	5	1	2	2	1	1	1	2	31

TABLE 4—*Duration of Symptoms in Days*

	1	2	3	4	5	14	Total
1 Irrationality	5	3	2	2	1		13
2 Irritability	4	1	1		1		7
3 Vomiting	5	4			1	1	11
Total	14	8	3	2	3	1	31

TABLE 5—*Mortality in Relation to the Lobe Injured*

Type of Injury	Right Lobe			Left Lobe		
	No of Patients	Died	Lived	No of Patients	Died	Lived
Stab	5	3	2	4	0	4
Trauma	8	7	1	2	2	0
Bullet, clean wound	9	5	4	6	3	3
Bullet, macerating wound	17	9	8	7	6	1
Total	39	24	15	19	11	8

The right lobe was involved in thirty-nine cases, the left lobe in nineteen and both lobes in two. In two thirds of all the fatal cases there was injury to the right lobe (table 5).

In forty-one cases the liver was the only organ involved. In the cases of injury to the right lobe there was higher mortality. The deep wounds caused all the deaths, the seven patients suffering from superficial wounds lived even when severe hemorrhage was present (table 6).

*Other Organs Involved*—In twenty-one cases other organs were involved, in all these the injury was caused by gunshot, except in one,

the important observation that calcification of epiphyseal cartilage in rickets took place in normal serum but not in rachitic serum, Robison and Soames<sup>13</sup> and Shipley, Kramer and Howland<sup>14</sup> found that it similarly occurred in artificial fluids in vitro. The calcification is analogous to spontaneous healing in rickets and takes place in the presence of adequate calcium and phosphorus ions, at an appropriate  $p_H$  at body temperature. It does not occur<sup>14</sup> in the icebox and is inhibited by a number of factors, such as soaking in chloroform, ether or solution of formaldehyde, the presence of magnesium ions,<sup>15</sup> an increase of total ions in solution,<sup>16</sup> the presence of dextrose<sup>17</sup> and heating to a temperature of 60 C for ten minutes.

It was by the use of rachitic cartilage in vitro as an indicator that Robison proved the presence of the monophosphoric esterase, phosphatase, in calcifying cartilage.<sup>18</sup> Robison pointed out that there were two mechanisms involved in the formation of rachitic epiphyseal cartilage: (1) the monophosphoric esterase and (2) a mechanism concerned with local deposition from a supersaturated solution in the selective way that occurs in healing rachitic cartilage in vivo, crudely expressed as "the line test."

An important advance recently achieved by Robison and Rosenheim<sup>17</sup> was the successful deposition of a line of strontium in rachitic epiphyseal cartilage in vitro from an inorganic solution in which strontium replaced the calcium ions. This is experimental evidence that the deposition from inorganic solutions is not a specific effect of calcium and further that any difficultly soluble salt in a faintly alkaline medium is biologically precipitable as a bone salt.

#### MECHANISM OF PRECIPITATION OF INORGANIC SALTS IN BONE

Beyond the fact that bone contains a phosphoric esterase<sup>18b</sup> in large amount, even at a bone age of less than 24 hours,<sup>19</sup> nothing is known about the mechanism of calcification in mammalian bone. However, Fell and Robison<sup>20</sup> successfully cultivated in vitro the isolated femur

13 Robison, R., and Soames, K. M. *Biochem J* **18** 740, 1924.

14 Shipley, P. G., Kramer, B., and Howland, J. *Biochem J* **20** 379, 1926.

15 Shipley, P. G., and Holt, L. E. *Bull. Johns Hopkins Hosp.* **41** 437, 1927.  
Kramer, B., Shelling, D. H., and Orent, E. R. *ibid.* **41** 426, 1927. Robison, R., MacLeod, M., and Rosenheim, A. H. *Biochem J* **24** 1927, 1930.

16 Shelling, D. H., Kramer, B., and Orent, E. R. *J. Biol. Chem.* **77** 157, 1928.

17 Robison, R., and Rosenheim, A. H. *Biochem J* **28** 684, 1934.

18 Robison, R. (a) *Biochem J* **17** 286, 1923, (b) *The Significance of Phosphoric Esters in Metabolism*, New York: New York University Press, 1932.

19 Huggins, C. B. *Biochem J* **25** 728, 1931.

20 Fell, H. B., and Robison, R. *Biochem J* **23** 767, 1929.

vessels Repeated or continuous hemorrhage continues the stimulation until a point is reached after which no therapy is successful Early replacement of an adequate amount of fluid is necessary and promptly gives good results His experiments pointed out that transfusion of blood or administration of a 6 per cent solution of acacia gives the best results This work also contraindicated the giving of medicinal stimulants, especially epinephrine

TABLE 9—*Hemorrhage in Relation to the Degree of Injury*

	Slight	Moderate	Severe	Death	Recovery
Stab	0	2	7	3	6
Trauma	0	0	10	9	1
Clean bullet wounds	1	4	10	8	7
Macerated bullet wounds	1	3	22	17	9
Superficial bullet wounds	1	2	4	0	7

TABLE 10—*Mortality Caused by Various Agents*

Agent	Died	Lived
Gunshot	25	16
Stab	3	6
Trauma		
Automobile	8	1
Fall	1	
Total	37	23

TABLE 11—*Complications Causing Death*

	24 Hrs	48 Hrs	72 Hrs	4 Days	5 Days	6 Days	7 Days	8 Days	9 Days	19 Days	21 Days
Hemorrhage and shock	20	3	4	1							
Toxic (bile) peritonitis					1	3		1		1	1
Infective peritonitis							1				
Mediastinal pressure									1		
Total	20	3	4	1	1	3	1	1	1	1	1

*Mortality and Cause of Death*—The mortality in the entire series was 61.6 per cent, the mortality in cases in which operation was performed was 56.6 per cent, and that in cases in which there was no operation was 60 per cent Table 10 shows the relation between the agent of trauma and the mortality

Hemorrhage and shock caused death in 73 per cent of the cases in which they occurred, and all the patients died within three days, only a few living longer than twenty-four hours Because all these cases were "coroner's cases," autopsy was performed by us in only three A number of deaths termed "toxic deaths" probably belong to the "bile peritonitis" group because they resembled them clinically in all details (table 11)



The present experiments were concerned with two questions (1) whether a local calcium deposition stimulates osteogenesis and (2) the nature of the epithelial osteogenetic stimulus

#### THE INFLUENCE OF LOCAL CALCIUM DEPOSITS ON OSSIFICATION

The evaluation of the importance of a local calcium deposit as an osteogenetic stimulus is difficult. It seems plain that the solid phase of the bone salt facilitates further deposition from a supersaturated solution of calcium with phosphate and other anions concerned in apatite formations. From a biologic standpoint, formation of bone adjacent to calcified tubercles, fibroids, atheromatous plaques and renal calculi<sup>28</sup> is not an uncommon observation. Moreover, the presence of bone salt deposition in the scaffolding of calcified cartilage in bones which pass through a chondrial stage apparently facilitates replacement of the cartilage by bone, but in what manner this takes place it is impossible to say at present. Since bone forms in the skull and clavicle without a calcified precursor, it is known that a calcified deposit is not an absolute prerequisite. From an experimental standpoint, calcium salts have apparently led to formation of bone in two instances. Barth<sup>29</sup> implanted ashed bone in the peritoneal cavity of the cat and observed new formation of bone closely adjacent. Similarly, Wurm<sup>30</sup> observed bone three months after implantation of a calcium phosphate-calcium carbonate mixture in young rabbits, after completely negative results had been observed in older animals.

These experimental observations showing that bone has formed away from the skeleton, however, have not been confirmed by the experience of most workers, notably Morpurgo and Martini, Lick, Pochhammer, Rhode and others<sup>31</sup>. The issue is somewhat clouded by the results of experimental implantation of calcium salts in an artificial bone defect, since it is difficult to tell how much new formation of bone arises from the original skeletal elements growing along and through the implanted inorganic salts and how much arises from direct action of these salts on nonskeletal fibroblasts. Thus Albee and Morrison,<sup>32</sup> Murray,<sup>33</sup> Cretin<sup>34</sup> and others expressed the belief that inorganic salts facilitate the healing of artificially created bone defects. On the other hand,

28 Huggins, C. B. Bone and Calculi in the Collecting Tubules of the Kidney, *Arch Surg* **27** 203 (July) 1933. Phemister, D. B. *Ann Surg* **78** 239, 1923.

29 Barth, A., cited by Wurm<sup>31</sup>.

30 Wurm. *Verhandl d deutsch path Gesellsch* **25** 191, 1930.

31 Cited by Wurm, H. *Beitr z path Anat u z allg Path* **85** 401, 1930.

32 Albee, F. H., and Morrison, H. F. *Ann Surg* **71** 32, 1920.

33 Murray, C. R. *J Dent Research* **11** 837, 1931.

34 Cretin, A., cited by Haldeman and Moore<sup>37</sup>.

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## EXPERIMENTS ON THE THEORY OF OSTEOGENESIS

THE INFLUENCE OF LOCAL CALCIUM DEPOSITS ON OSSIFICATION,  
THE OSTEOGENIC STIMULUS OF EPITHELIUM

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AND

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CHICAGO

Despite the numerous experimental data acquired especially since 1923, there are still defects in the knowledge of calcification in normal tissues, that is in calcified cartilage, teeth and bone. During this twelve year period, great advances in the subject have been made, much greater confidence is now held in the ideas of the state of calcium in the circulating blood and of the nature of the bone salts. Moreover progress has been made in elucidating mechanisms by which transference is accomplished from the former a liquid phase, to the solid phase found in calcified normal tissue. The importance of these mechanisms is obvious. It is elementary but axiomatic that improvements in knowledge of biologic mechanisms are reflected in improved clinical efficiency.

The purpose of the present communication is to indicate briefly some of the recent advances in this field and to present several experiments which perhaps integrate the subject further.

### NATURE OF THE BONE SALT

The organic matrix of bone is little understood. As far as is known it consists of the same collagen that is present in common connective tissue and cartilage<sup>1</sup> together with an albuminoid and mucoid, the organic fraction contains a protein constituent with reducing characteristics, not precipitated by tri-chloroacetic acid and soluble in acetone. Great advances have been made in understanding the nature of the inorganic bone salt, especially by the use of roentgen spectography. The principle of this method is that crystalline aggregates cause diffraction of roentgen rays with the production of a spectrum typical for each

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<sup>1</sup> Morner, C T. *Ztschr f physiol Chem* 20:237, 1895. Hawk P B, and Gies, W J. *Am J Physiol* 5:387, 1901.

3 Implantation of inorganic salts in the skull led to a slightly different result, in that in specimens examined four, six and eight weeks after implantation the new processes of bone which formed at the cut margins of the trephine defect were observed growing over the implant, and in several instances appositional replacement<sup>40</sup> occurred

*Comment*—The conclusion was reached that apatite implants of bone did not stimulate the connective tissue of the abdominal wall to form bone in the length of time in which these implants were present before



Fig 1—Section ( $\times 30$ ) showing transplant of deciduous tooth to abdominal muscles in a dog, sixty-three days after operation. New bone formation is shown in the fibroblasts filling the pulp canal

complete absorption took place. The absence of giant cells during the resorptive process was a noteworthy feature.

*EXPERIMENT 2—New formation of bone by transplantation of teeth to the abdominal wall*

*Method*—In ten young dogs between 6 and 9 weeks of age under ether anesthesia the deciduous canine tooth was painted with tincture of iodine and ampu-

<sup>40</sup> Barth, A. Arch f klin Chir 46 409, 1893. Marchand, F. Der Process der Wundheilung, Stuttgart, Ferdinand Enke, 1901.

bonate by referring it to the low plasma bicarbonate concentration of the blood in these species. As Morgulis pointed out, this observation militated against the view that the carbonate apatite is the principal crystallite deposited in normal tissues. The distribution of the apatites in the bone of the fish seemingly is dependent on the constitution of the circulating blood, and presumably larger amounts of oxyapatite and hydroxyapatite are present in fishes than in mammals, in which the high plasma bicarbonate accounts for carbonate apatite deposits.

The blood serum under abnormal conditions similarly affects the mineral composition of bone. While normally the principal cations present are calcium and magnesium, in poisoning others, such as the salts of lead, strontium, silver, radium and related salts, like thorium,<sup>10</sup> form in bone, reflecting their presence in the blood stream. Moreover insoluble lakes such as are formed between alizarate and calcium accumulate in bone when they are present in the blood stream. There is another class of substances which from their chemical behavior throw light on the deposition mechanism, that is, the accumulations of urates in bone in gout. In this case the cation is soluble and the anion very slightly soluble at physiologic hydrogen ion concentrations in the tissues, and nevertheless the urate accumulates at certain areas in bone.

The conclusion, then, is that the inorganic constitution of bone is influenced by the composition of the body fluids, and under normal conditions the predominant salts are of the apatite group, which may be expressed by the formula of de Jong, but that under abnormal conditions other salts accumulate and that any chemical combination which tends to make an insoluble or difficultly soluble salt in a faintly alkaline watery medium will be found in bone and teeth.

#### THE STATE OF CALCIUM IN THE BODY FLUIDS

Using a biologic method which depended on the sensitivity of the heart of the frog for calcium ions, McLean and Hastings<sup>11</sup> discovered that total calcium, total protein and calcium bound to protein are all interrelated in an equilibrium which as a first approximation can be represented by a simple mass law equation. In other words, the amount of ionized calcium is greatly influenced by the protein concentration of plasma.

#### MECHANISM OF DEPOSITION OF APATITE SALTS IN CARTILAGE

Significant data have been accumulated on the deposition of apatite salts in cartilage, especially on calcification *in vitro*. Shipley<sup>12</sup> made

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10 Behrens, B, and Baumann, A. *Ztschr f d ges exper Med* **92** 251, 1933

11 McLean, F C, and Hastings, A B. *Proc Soc Exper Biol & Med* **30** 1344, 1933, **31** 529, 1934

12 Shipley, P G. *Bull Johns Hopkins Hosp* **35** 304, 1924

2 Implantation of Boiled Deciduous Teeth A similar encapsulation of the tooth and filling in of the pulp cavity with newly formed connective tissue were found In every case there was complete absence of bone (fig 3), although unboiled teeth from the same animal constantly contained deposits of new bone In these implants of deciduous teeth the enamel was apparently undisturbed by resorptive changes which affected the dentin

3 Implantation of Unboiled Unerupted Teeth In this experiment bone was found in the pulp space in seven of ten teeth implanted in the abdominal wall,

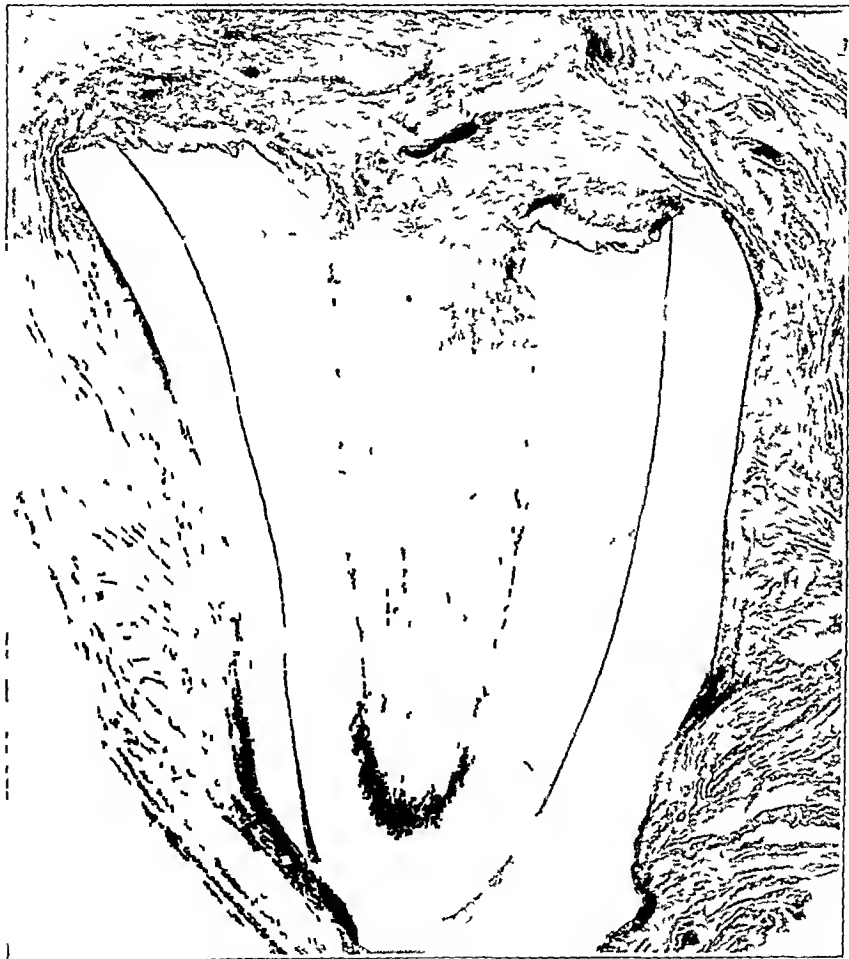


Fig 3—Section ( $\times 30$ ) showing transplant of a boiled deciduous tooth to abdominal muscles, sixty-three days after operation No bone formation is present

although it was less in amount than in the deciduous teeth In three cases an interesting creeping substitution of the enamel occurred (fig 4)

*Comment*—This experiment is interpretable from two obvious standpoints Either the apatite salts of tooth which are identical with the inorganic bone salt<sup>4</sup> act as a local stimulus to fibroblasts or tooth cells are carried over in the transplantation and form bone Since

from 5½ and 6 day fowl embryos, and bone formed in their tissue cultures, the phosphatase content was low at the time of explantation and increased greatly at the time of calcification. The mechanism of calcification in bone differs appreciably from that of calcification of hypertrophic cartilage in that, as stated, cartilage calcifies in vitro under favorable conditions whereas osteoid does not calcify under the conditions which are effective for calcification of cartilage.

The question whether the osteoblast is or is not a specific type of cell endowed with specific functional characteristics seems to be settled in the affirmative. The opinion most recently stated by Jones and Roberts,<sup>21</sup> and previously advocated by LeRiche and Policard,<sup>22</sup> that the osteoblast cannot be regarded as a cell endowed with the specific power of laying down bone and that the bone cell is a fibroblast imprisoned in bone in a state of quiescence, can easily be shown to be erroneous, and further data in this regard will be presented later. The evidence shows that the osteoblast is derived from cells of the fibroblast series and that it differs from its precursors, although more from a physiologic than from an anatomic standpoint.

It was shown<sup>23</sup> in the dog that ossification occurs readily in certain fibroblast areas under the influence of the epithelium of the urinary tract. These observations derived from surgical methods have been confirmed by several groups of workers.<sup>24</sup> The mechanism by which epithelial cells influence certain fibroblasts to produce bone is unknown, except for phosphatase determinations<sup>25</sup> and the failure of an extract of bladder mucosa to form bone,<sup>24b</sup> no chemical facts are known about this effect, which is still in a descriptive physiologic state. A similar effect has been found in the mucosa of the gallbladder in the dog and the guinea-pig<sup>26</sup> and in germ elements of teeth.<sup>27</sup>

21 Jones, R. Watson, and Roberts, R. E. *Brit J Surg* **21** 461, 1934.

22 LeRiche, R., and Policard, A. *The Normal and Pathological Physiology of Bone*, translated by S. Moore and J. A. Key, St. Louis, C. V. Mosby Company, 1928.

23 Huggins, C. B. (a) *Proc Soc Exper Biol & Med* **27** 349, 1930, (b) *The Formation of Bone Under the Influence of Epithelium of the Urinary Tract*, *Arch Surg* **22** 377 (March) 1931.

24 (a) Abbott, A. C., and Goodwin, A. M. *Canad M A J* **26** 393, 1932. (b) Copher, G., Key, J. A., and West, E. S. *Proc Soc Exper Biol & Med* **29** 646, 1932. (c) Roome, N. W., and McMaster, P. E. *Influence of Venous Stasis on Heterotopic Formation of Bone*, *Arch Surg* **29** 54 (July) 1932. (d) Regen, E. M., and Wilkins, W. E. *J Lab & Clin Med* **20** 250, 1934. (e) LeRiche, R., and Lucinisco, E. *Presse med* **43** 137, 1935. (f) Jung, A., and Cemil, S. *ibid* **43** 140, 1935.

25 Huggins<sup>19</sup> Regen<sup>24d</sup>

26 Huggins, C. B., and Sammett, J. F. *J Exper Med* **58** 393 1933.

27 Huggins, C. B., McCarroll, H. R., and Dahlberg, A. A. *J Exper Med* **60** 199, 1934.

described as invading dentin and enamel in the fashion known as creeping substitution. Hojer<sup>42</sup> and Wolbach and Howe<sup>43</sup> similarly noted formation of bone (osteodentin) in the pulp in cases of vitamin C and vitamin A deficiency, which shows that under this abnormal circumstance the odontoblasts lose histologic polarity and act as osteoblasts



Fig 5—Roentgenogram of a spleen in which four pieces of epithelium of the urinary bladder had been transplanted in the upper two thirds with no bone formation, while in the lower pole, where epithelium and sheath of the rectus abdominis muscle were transplanted together, bone was formed at fifty-seven days. The arrow points to the bone density.

42 Hojer, J. A. *Acta pædiat (supp)* 3 8, 1924

43 Wolbach, S. B., and Howe, P. R. *Am J Path* 9 275, 1933

Eden,<sup>35</sup> Key,<sup>36</sup> Haldeman and Moore<sup>37</sup> and Brunschwig and Harmon,<sup>38</sup> representing a majority of the investigators in this field, reported that the solid bone salts have no or slight influence on the production of new bone. Furthermore, as pointed out by Brunschwig and Harmon,<sup>39</sup> the fact that certain skeletal tumors ossify together with all metastases strongly indicates the presence of a specific cell type, the osteoblast.

#### EXPERIMENTAL DATA

**EXPERIMENT 1**—*Implantation of bone salts in abdominal wall surgical defect in rib and trephine defect in skull*

**Method**—The femur and skull of a 1 year old dog were sawed into segments 2 cm in length, and these were boiled in a 5 per cent solution of potassium hydroxide for three days, the alkali being changed repeatedly, until the organic framework was completely hydrolyzed. The completeness of hydrolysis was determined by the absence of nitrogen as determined by the Kjeldahl method. The masses of bone were then washed for two days in running water until they exhibited a neutral reaction, then they were sterilized in an autoclave.

With the animal under ether anesthesia, aseptic precautions being used, this deproteinized bone was implanted (1) between the external oblique and the internal oblique muscle of the abdomen in twelve dogs, (2) in a 2 cm defect following subperiosteal costectomy in six dogs, (3) in a defect produced by a crown trephine in the parietal bone of the skull in six dogs. The wounds were closed with fine silk. The animals were killed at two week periods, beginning two weeks after operation.

**Results** 1 Implantation of deproteinized bone into the abdominal wall did not lead to new formation of bone in any instance, the implant was gradually absorbed. In the two week specimen many of the channels which had contained blood vessels before alkaline hydrolysis were already filled with new blood vessels. The inorganic salts had become infiltrated with protein, so that after decalcification of the specimen by hydrochloric acid a protein framework was left. The osteocyte spaces were not infiltrated by cells. The mass was surrounded by a capsule of fibrous tissue. Noteworthy was the absence of giant cells.

Specimens examined four, six and eight weeks after implantation showed similar features, it was difficult to prove absorption of the inorganic salts up to this time, although it was believed that it had occurred. In specimens examined ten, twelve and fourteen weeks after implantation the absorptive process was clearly seen, there had occurred fragmentation of the bone salt implants. After sixteen and eighteen weeks only traces of the implants were detectable.

2 Implantation in a costal defect led to encapsulation of the inorganic salt mass by fibrous connective tissue, with partial extrusion of the mass out of contact with the rib and partial resorption in each case. No sign of formation of new bone was observed.

35 Eden, R. *Klin Wchnschr* 2 1798, 1923

36 Key, J. A. *J Bone & Joint Surg* 16 176, 1934

37 Haldeman, K. O., and Moore, J. M. Influence of Local Excess of Calcium and Phosphorus on the Healing of Fractures. An Experimental Study, *Arch Surg* 29 385 (Sept) 1934

38 Brunschwig, A., and Harmon, P. H. *Am J Cancer* 22 342 1934

39 Brunschwig, A. and Harmon, P. H. *Surg, Gynec & Obst* 57 711, 1933



A similar change of tooth cell to osteoblast type is predicated in the present experiment, in which the tooth was transplanted from its normal environment to the abdominal wall

**EXPERIMENT 3**—*Transplantation of the epithelium of the urinary bladder to the abdominal fascia in the rat and guinea-pig, resulting in osteogenesis*

**Method**—In four rats and three guinea-pigs under ether anesthesia, the peritoneal cavity was opened, the urinary bladder exposed and the dome amputated

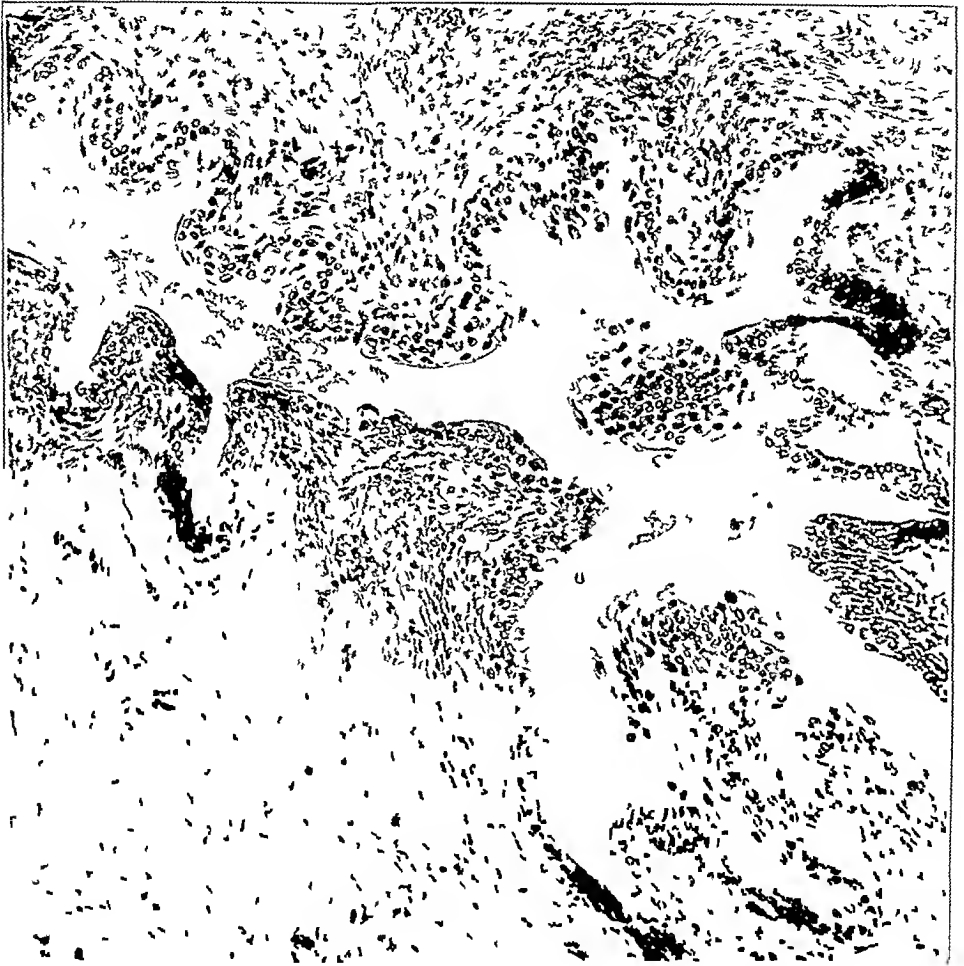


Fig 7—Section ( $\times 140$ ) showing vesical epithelium alone transplanted to the spleen at forty-seven days there is absence of bone formation, although the epithelium is surrounded by fibroblasts

The excised epithelium was then sutured on the external oblique muscle. Closure of the bladder was effected with a purse-string suture of fine silk placed in the layers of muscle, infolding the cut surface.

**Results**—In each case the transplant survived and formed a cyst, which was partly surrounded by a plaque of bone. The results correspond in every way with the findings in a similar experiment on the dog.<sup>23b</sup>

tated with a hollow rongeur, at a point about 3 mm distal to the margin of the gum. It was found that with practice this could be done without splintering the tooth. Maintaining this distance from the margin of the gum without splintering the tooth assured the absence of bone cells in the transplant. In four anesthetized pups of the same age an incision was made in the mucosa overlying the permanent unerupted canine tooth, this was exposed, the membranes were opened, and the tooth was extracted. In both the permanent and the deciduous teeth the pulp was gently lifted out and discarded. At least two teeth of each dog were thus obtained, and one of the pair was boiled for ten minutes in water to assure death

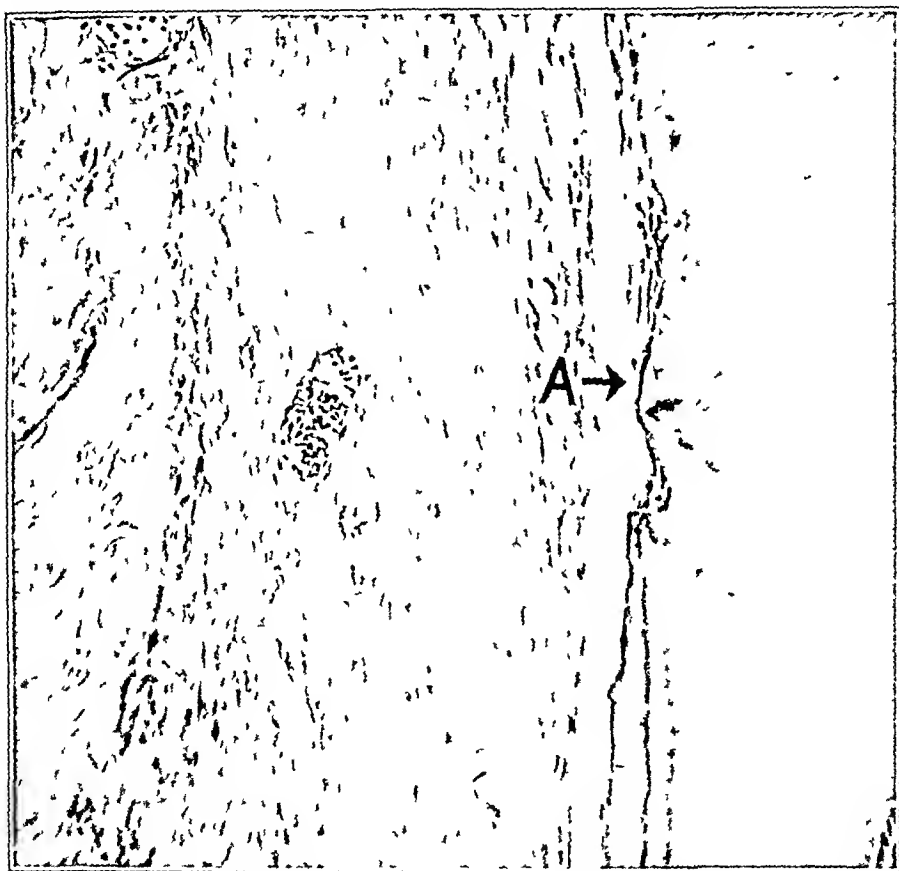


Fig 2—Higher magnification ( $\times 250$ ) of the section presented in figure 1, showing a portion of the pulp canal, with creeping substitution of dentin at A

of the cells. The teeth were implanted in the abdominal wall, between the internal and the external oblique muscle. The specimens were recovered between thirty-five and sixty-three days after implantation.

**Results**—1 **Implantation of Normal Deciduous Teeth** In each case fibrous connective tissue was found filling the pulp space of the tooth, and always new bone was found, usually in this tissue (fig 1), but in four teeth there was no ossification in the pulp space. In every case there was found oppositional substitution of the dentin by bone (fig 2). The tooth was encapsulated by fibrous connective tissue. In two teeth infection was present, and in these teeth the amount of new bone was small.

this technic there was no wound of the peritoneum closer to the patch than these needle holes. Typical bone formed, and a curious effect was achieved. Mucosa and connective tissue were seen growing along the threads as well as becoming locally adherent, the bone formation recovered consisted of a solid plaque the shape of the original patch, with four bony processes corresponding to the threads.

#### COMMENT

Experiments 1 and 2 show clearly that a local calcium depot is not a rapid stimulus for the formation of bone. To be reconciled with the experimental data, however, is the fact that frequently bone occurs in old calcified lesions. The explanation of this phenomenon may be found possibly in the fact that a longer period is necessary for apatite calcification to effect ossification than occurred in the present experiments, and hence that apatite salts may serve as a slow indolent stimulus to ossification. A separate explanation that may be provided is that the bone observed in pathologic conditions developed at the time of the original calcification and survived.

The experiments in which bone was formed as a result of the epithelial stimulus show that the same mechanism is at work in the guinea-pig and rat as in the dog, the epithelium that lines the urinary bladder of these animals is an osteogenic membrane. Ossification is prevented by a functional difference between connective tissues. It is interesting that the outer fibroblasts of the subperitoneal coat of the urinary bladder are not capable of resisting the bone-forming stimulus of the epithelium of the bladder, while the fibroblasts in the interior of the bladder must invariably resist it, the formation of bone in the urinary bladder has not been described, except in the Neuhof patches.<sup>45</sup>

#### SUMMARY

1 Transplantation of bone, hydrolyzed in strong alkali to destroy the organic elements, to the abdominal muscles and to replace defects in the skull and ribs did not stimulate the formation of new bone.

2 Transplantation of deciduous teeth to the abdominal muscles led to the formation of bone in these teeth. Boiling completely inhibited the formation of bone.

3 Epithelium of the urinary bladder transplanted to the abdominal wall in the rat and the guinea-pig led to formation of cysts and production of bone.

4 In the dog, epithelium of the urinary bladder transplanted into the spleen did not lead to formation of bone unless connective tissue capable of ossification was transplanted with it. Transplantation to the surface of the spleen led to the formation of a small amount of new bone in several cases.

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45 Neuhof, H. Surg., Gynec. & Obst. 24: 383, 1917.

boiling in water does not affect the inorganic salts and since it abolishes the formation of bone, it appears reasonable to ascribe the new bone to transplanted tooth cells rather than to the solid calcified phase.

The formation of bone in dental pulp tissue has been observed not infrequently,<sup>41</sup> after retention in the jaw of an unerupted tooth, fracture of a tooth, reimplantation, infection, etc. The bone has also been



Fig 4—Section ( $\times 250$ ) showing creeping substitution of enamel by bone in an unerupted permanent tooth transplanted to the abdominal wall, after thirty-eight days

<sup>41</sup> Zuckerkandl, E. *Med Jahrb*, 1885, p 1. Romer, O. in Henke, F., and Lubarsch, O. *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer 1928, vol 4, pt 2, p 309. Coolidge E D. *J Am Dent A* 16 821, 1929, 15 1623, 1928. Worman H C. *ibid* 16 1885, 1929. Willman, W. *ibid* 17 444 1930. Boulger, E P. *ibid* 18 988, 1931.

# RELATION OF PATHOLOGIC CHANGES OF THE INTERVERTEBRAL DISKS TO PAIN IN THE LOWER PART OF THE BACK

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NEW YORK

My purpose in this presentation is to direct attention to a consideration of the importance of pathologic changes of the intervertebral disks, particularly those of the lower lumbar portion of the spine and of the lumbosacral junction, in the causation of pain in the lower part of the back. The intervertebral disks have until recently escaped careful investigation. Although the literature is full of papers on pain in the lower part of the back, they are, on the whole, concerned with the presentation of new theories, diagnostic procedures and methods of treatment. Few investigators have attempted to study the underlying pathologic condition. Schmorl<sup>1</sup> was the first to undertake a careful and comprehensive study of the intervertebral disks at autopsy. His contributions have greatly increased the knowledge of the anatomy and pathology of the disks.

## ANATOMY

The normal adult intervertebral disk consists of a circumferential fibrous ring, called the annulus fibrosus, a highly expansile nucleus pulposus and two thin plates of hyaline cartilage. In the living state the nucleus is compressed by the contiguous plates of cartilage and the vertebral bodies and is prevented from expanding laterally by the annulus fibrosus. The annulus fibrosus consists of firm fibrous strands circumferentially arranged around the periphery of the body and surrounding the nucleus pulposus. The nucleus pulposus and the annulus fibrosus comprise the main substance of the intervertebral disks and are separated from the vertebral bodies by the two thin plates of hyaline cartilage (fig 1).

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From the Orthopedic Service of Dr H Finkelstein, Hospital for Joint Diseases

1 Schmorl, G. Ueber die an den Wirbelbandscheiben vorkommenden Ausdehnungs- und Zerreissungsvorgänge und die dadurch an ihnen und der Wirbelspongiosa hervorgerufenen Veränderungen, Verhandl d deutsch path Gesellsch **22** 250, 1927, Ueber Knorpelknötchen an den Wirbelbandscheiben, Fortschr a d Geb d Röntgenstrahlen **38** 265, 1928, Ueber die pathologische Anatomie der Wirbelbandscheiben, Beitr z klin Chir **151** 360, 1931



Fig 6—Section ( $\times 140$ ) of vesical epithelium and sheath of the rectus abdominis muscle transplanted to the spleen, at forty-seven days, showing formation of bone strictly confined to the transplant

bodies to beginning vascular infiltration of the substance of the disk, fibrous replacement of nuclear tissue, brown degeneration, calcification of the nucleus, and, in late stages, shrinkage narrowing and ossification of the disk (figs 2 and 3) In a sagittal section of an adult spine one or more of these changes may be noted in the disks Because of the lack of mobility of the dorsal portion of the spine, these changes take place early and gradually lead to complete absence of motion

In the lumbar region, because of the size strength and increased mobility of the disks, the pathologic changes of the disk substance have

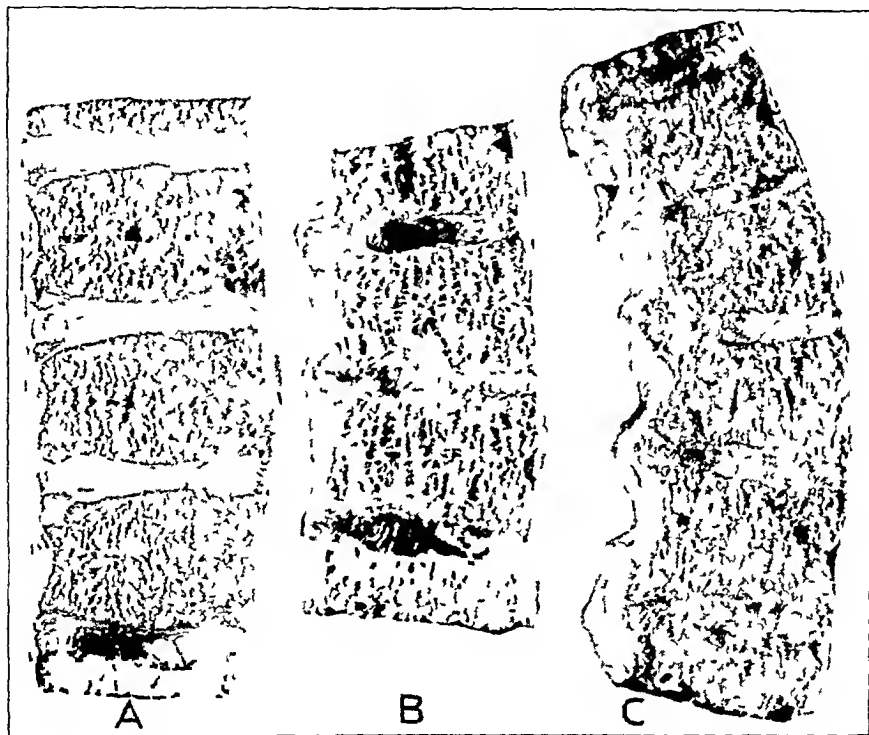


Fig 2—In *A* may be seen discoloration and beginning degeneration of the lowest disk, *B* shows advanced degenerative changes, with herniations and narrowing of the disks, and *C*, degenerative changes, with ossification of the disks anteriorly

a pronounced effect on the functional activity and resistance of the spine When degenerative changes are present in the lower lumbar and lumbosacral intervertebral disks, the flexibility and mobility of the spine are considerably diminished, and its capacity to withstand the strain and shocks of functional activity is greatly reduced

When a sagittal section of the spine is examined post mortem, one frequently finds herniation from the disks into the adjacent bodies These invasions are usually of small size but often may extend for a

EXPERIMENT 4—*Transplantation of mucosa of the urinary bladder to the spleen*

*Method*—In sixteen dogs, a large area of the mucosa of the bladder was isolated as previously described and the bladder closed. The strip of mucosa was then treated variously: (1) transplanted to the interior of the spleen, (2) sutured to a piece of connective tissue of similar size from the sheath of the rectus abdominis muscle, both tissues being transplanted together to the spleen, or (3) sutured on the surface of the spleen. Autopsy was performed between fifty and seventy-two days after the operation. Serial histologic sections were made of the transplant.

*Results*—As previously reported,<sup>23b</sup> it was found that when mucosa of the bladder alone was transplanted to the spleen it survived and became surrounded by connective tissue but no ossification resulted, although when mucosa of the bladder was transplanted to the spleen with a connective tissue susceptible of ossification, such as the sheath of the rectus abdominis muscle (fig 6), bone invariably formed.<sup>44</sup> However, when mucosa of the bladder was transplanted on the surface of the spleen, tiny spicules and traces of bone were found in four of six cases, the changes being observed by the use of serial sections.

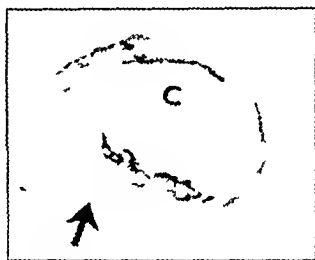
EXPERIMENT 5—*Transplantation of mucosa of the urinary bladder to the peritoneum*

Fig 8—Roentgenogram of a specimen in an experiment in which vesical mucosa was transplanted to the external posterior surface of the same bladder for forty-nine days. The cyst (C) which formed with bone in the outer coat of the bladder may be seen. The arrow points to the mucosa of the bladder lumen.

*Methods*—In nineteen dogs under ether anesthesia, large segments of mucosa of the bladder were elevated in the manner described and transplanted to various parts of the peritoneal cavity: (1) to the omental apron, which was then rolled up and sutured so that the transplant did not come in contact with the parietal peritoneum, (2) to the posterior surface of the urinary bladder, and (3) to the parietal peritoneum. Autopsy was performed from forty-nine to eighty-four days after the operation.

*Results*—In every case bone was found. In the omentum, the bladder mucosa proliferated and formed a cyst partly surrounded by a plaque of bone immediately beneath the epithelium. On the outside of the bladder, similarly, a cyst was found with bone in the subperitoneal coat of the bladder (fig 8). Likewise, in transplants to the parietal peritoneum bone was observed adjacent to the cyst in the connective tissue. The experiment was modified by fixing the epithelial patch in place with four long threads of silk anchored to the patch and entering the peritoneum 4 or 5 cm from the patch, where they penetrated the abdominal wall, by

<sup>44</sup> Huggins, C. B. Proc Inst Med Chicago 9:89, 1932.



Another consequence of a prolapse of the disk is that in large herniations a considerable portion of the matrix of the nucleus pulposus may extend into the body, resulting in shrinkage and narrowing of the disk substance. With a reduction in its size, movements in the disk are restricted, and stiffness results. Puschel,<sup>3</sup> in a study of the water content of a series of normal and degenerated intervertebral disks, found that the water content of the disks is greatest at birth and decreases with age. The figures for the degenerated disks are markedly lower than those for the normal ones.

Marked degenerative changes of the substance of the disk are often seen without any evidence of the herniation of the disk into the vertebral bodies or of extension of the disk into the spinal canal. These



Fig 4—Section through the fourth lumbar and the lumbosacral intervertebral disk, showing marked degenerative changes and narrowing of the disks. Note the disk node in the fourth lumbar body.

changes result from the general wear and tear of daily activity. They are more commonly seen in the aged and in men doing hard, laborious work. The lumbosacral disk, because of the increased strain, mobility and weight-bearing function to which it is subject, is a frequent site of early degenerative changes, with resulting shrinkage and narrowing of the disk (fig 4). With the onset of pathologic changes, the nucleus loses its normal elasticity and turgor, becoming firm, dense and immobile. The spine loses its flexibility, resilience and buffer function, and, as the process goes on, bony changes of the bodies become evident, with resulting stiffness of that part of the spine.

3 Puschel, J. Der Wassergehalt normaler und degenerierter Zwischenwirbelscheiben, *Beitr z path Anat u z allg Path* 84 123, 1930.

5 The peritoneum and adjacent fibroblasts, including the omentum, easily ossified under the epithelial stimulus. This led to the conclusion that the subperitoneal fibroblasts in the outer coat of the bladder differ from the fibroblasts adjacent to the lining epithelium of this structure in that the former ossify when in contact with bladder epithelium while the latter do not. The defense against the ossifying action of the epithelium of the urinary bladder thus is topographically confined to the inside of the bladder and is lacking in the outside coverings of this viscus.

may go on without any noticeable evidence of physical impairment or subjective complaints until a slight trauma, such as lifting a heavy object, a sudden twist or a misstep, precipitates a train of symptoms and physical signs that completely incapacitate the person. The trauma, although slight, is often sufficient to produce a compression of a pathologic disk.

A severe, sudden injury to the spine is an etiologic factor of far less frequency. An evidence of sudden, severe trauma is the finding of breaks in the cartilage plates and small fresh hemorrhages around the herniations from the disk (fig 5). The effect of the trauma depends not so much on the intensity of the traumatic agent as on the condition of the disk and its capacity to withstand it. With the exception of severe injuries that result in a fracture of the bone, an injury, such as a heavy blow or fall, which in a young person may give rise only

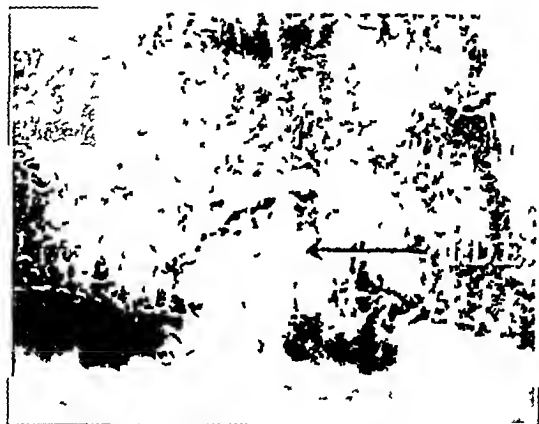


Fig 5—Low power photomicrograph of an extension of an intervertebral disk (IDE) into the proximal vertebral body. Note the marked vascular infiltration and dilatation of the vessels surrounding the disk node.

to slight discomfort, will result in pain and lengthy disability in an older person. The difference in resistance and adaptability is due in a large measure to the condition of the intervertebral disks. Thus in the young, the disks are expansile and possess a great capacity to absorb and "cushion" shocks and stresses, while in persons in late adult life, the disks are firm, their resilience is reduced and the cushion or buffer capacity is greatly diminished.

#### CLINICAL PICTURE

The clinical picture of the pathologic disks is not clearly demonstrable. There are no distinct signs or symptoms especially characteristic of this condition. The changes that occur are usually not isolated but are rather the result of the general process of wear and tear affecting the spine and other parts of the body. Arthritic changes of the

The disks form one quarter of the total length of the spine. They vary in size, being widest and thickest in the lumbar region and smallest in the dorsal region. In the lumbar region they form a third of its length.

The normal adult intervertebral disks have no blood vessels. They receive nourishment from the bone marrow of the bodies by diffusion.

The disks permit a considerable range of motion of the spine. Owing to the expansibility and turgor of the nucleus pulposus, the disks impart great flexibility to the spine. They act as a buffer or shock absorber for the strain and stress of daily activity. Mobility of the spine is greatest in the cervical and lumbar regions and least in the dorsal. Flexion is freest and most extensive in the lower lumbar portion of the spine. Goldthwait,<sup>2</sup> in 1910, determined that one half of the motion of the trunk below the lower dorsal region is made up of motion in

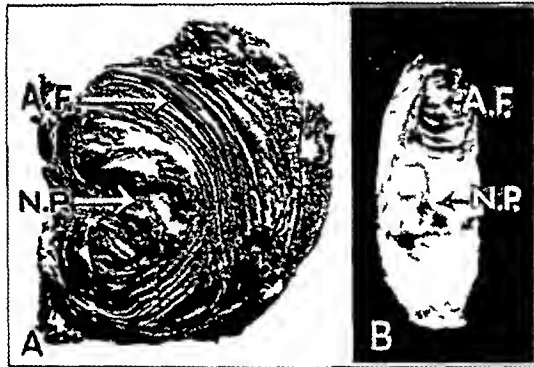


Fig 1— *A*, an intervertebral disk of the lumbar portion of the spine of an adult. Note the bulging nucleus pulposus (*N.P.*) surrounded by the circumferential fibrous ring, the annulus fibrosus (*A.F.*) *B*, cross-section of an adult lumbar intervertebral disk, showing the nucleus pulposus (*N.P.*) and the annulus fibrosus (*A.F.*)

the lumbosacral intervertebral disk and in the joint above it. The remainder of the motion is distributed between the rest of the lumbar portion of the spine and the sacro-iliac joints.

#### PATHOLOGY

Pathologic changes of the intervertebral disks are frequently noted at autopsy. They may be found after the first decade of life but are mainly seen after the third and increase in frequency with age. The changes vary from a small herniation from the disk into the vertebral

<sup>2</sup> Goldthwait J. E. The Lumbo-Sacral Articulation. An Explanation of Many Cases of "Lumbago," "Sciatica" and Paraplegia, Boston M & S J 164 365 (March 9) 1911

No forcible manipulation was used. In cases in which the spine was rigid and a fixed deformity was present, I did not attempt to correct it forcibly, but rather tried to obtain the best hyperextension position possible and to support the spine by means of a plaster of paris jacket or spica cast extending from the chest down to the toes of the involved leg.

#### REPORT OF CASES

CASE 1—H S, a white man aged 46, was admitted to the hospital with a complaint of pain over the lower part of the back and of radiating pain down the

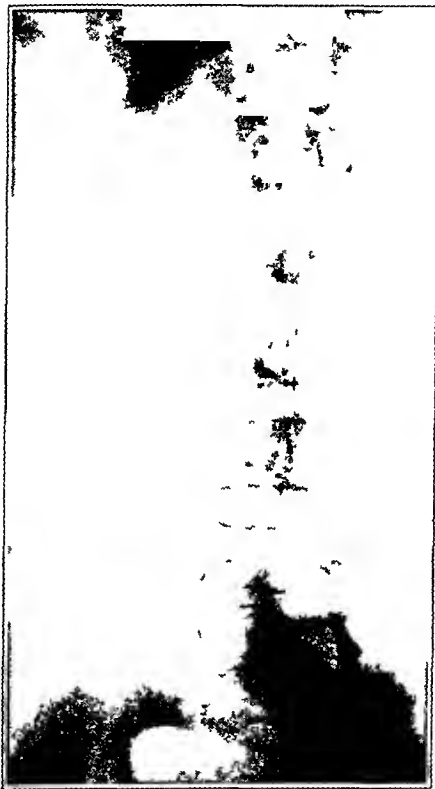


Fig 6 (case 1)—Oblique view, showing the narrowed lumbosacral intervertebral space with an increased lumbosacral angle

left leg. The condition came on suddenly four months before admission, while he was working.

*Examination*—The patient was well developed and well nourished. He walked guardedly, with his body tilted to the left. His spine was held rigid. Motion was restricted in all directions. There was tenderness over the lumbosacral junction and over the left sacro-iliac area. A straight leg-raising test gave negative results. The double thigh flexion test gave positive results. Hyperextension of the spine gave rise to pain over the lumbosacral region.

Anteroposterior, lateral and oblique roentgenograms revealed a narrowed lumbosacral intervertebral space, with an increase of the lumbosacral angle (fig 6).

*Treatment*—Under general anesthesia the lumbar portion of the spine was gradually hyperextended, reestablishing the normal lumbar lordosis. A plaster of

considerable distance into the substantia spongiosa. Schmorl<sup>1</sup> in an examination of three thousand spines, found herniation from the disks in 38 per cent of them.

The great majority of the herniations from the disks are not visualized by roentgen rays. They are seen only when a sclerosing layer of bone surrounds the disk or when there is a break in the cortical plate of the vertebral body. Their importance lies in the fact that with the

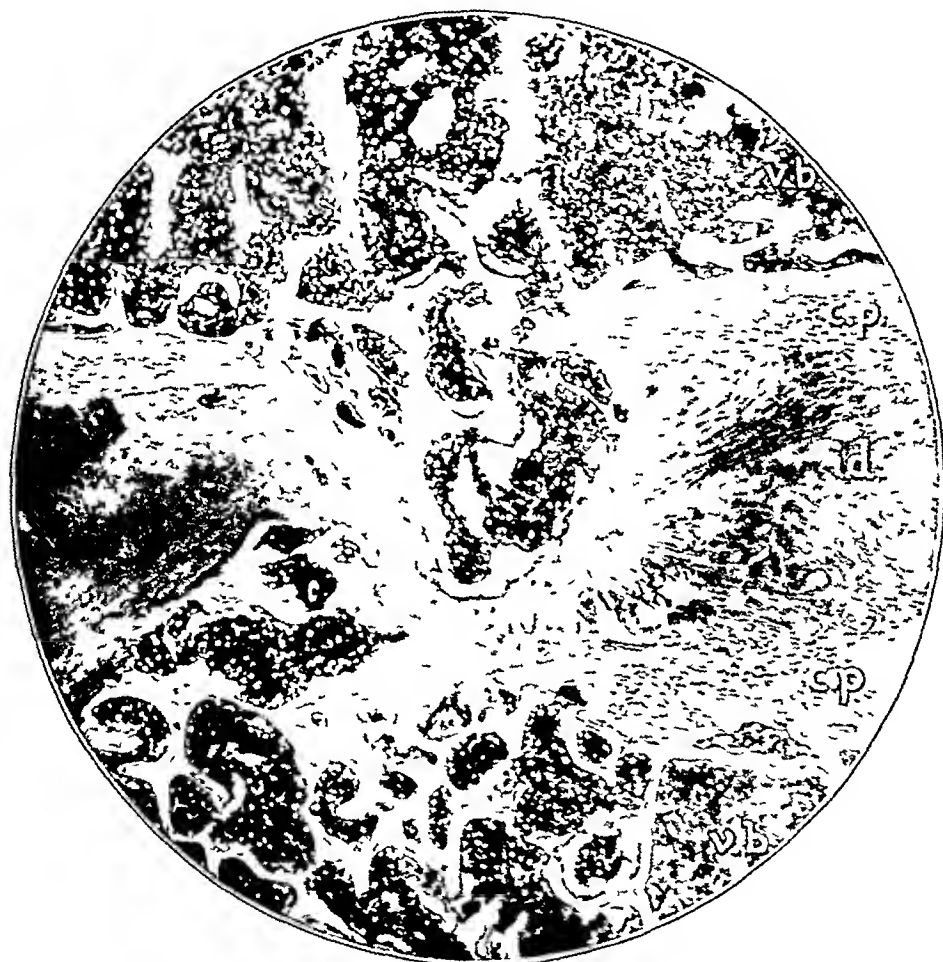


Fig 3—Low power photomicrograph of an intervertebral disk (*ld*) and adjacent vertebral bodies (*vb*) showing vascular infiltration and ossification of the disk. Note the break through the upper and lower cartilage plates (*cp*).

formation of a herniation from the disk an avenue is produced for the extension of blood vessels from the substantia spongiosa into the substance of the disk proper. With vascular infiltration the highly expansile gelatinous matrix of the nucleus pulposus is replaced by fibrous tissue. Gradual fibrillar degeneration with loss of fluid of the nucleus pulposus sets in resulting in the disk's shrinking and becoming firm.

down the back of the left limb. The condition came on insidiously eight months before admission.

*Examination*—The patient walked with a slight limp and with the spine tilted to the left. There was a slight left lumbar (sciatic) scoliosis. Motion of the spine was considerably restricted in all directions. There was tenderness over the right sacro-iliac region and the right gluteal region.

Roentgenograms revealed pronounced narrowing of the intervertebral disk between the fourth and the fifth lumbar body. The normal lumbar lordosis was obliterated (fig 8).

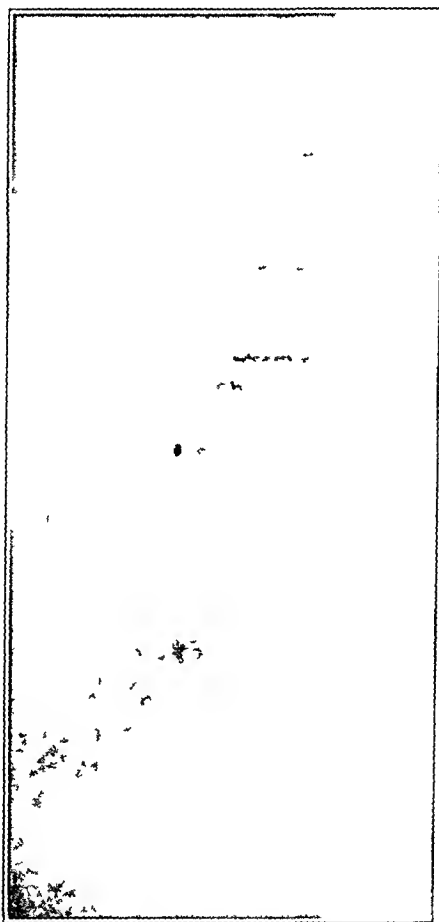


Fig 8 (case 3)—Pronounced narrowing of the fourth lumbar intervertebral space, with reversal of the normal lordosis to a slight kyphosis.

*Treatment*—Traction was applied on a convex frame for several weeks. Later the spine was hyperextended, and a plaster of paris corset was applied, holding the lumbar spine in slight lordosis.

**CASE 4**—M. M., a white man aged 50, came to the clinic complaining of pain over the lower part of the back and of shooting pains and numbness down the back of the left leg. The condition came on after a game of hand ball several months before admission.

*Examination*—The patient was obese and well developed. His spine was held rigid, with the body tilted to the right. He was unable to bear any weight on

When a partly macerated spine of a young adult with the intervertebral disks intact is carefully studied, one observes that the articular surfaces of the posterior articular facets are in close contact with and parallel to each other when the column of lumbar bodies is in slight lordosis. When one attempts to flex forcibly the lumbar portion of the spine, a slight compression of the disk occurs anteriorly and with it a slight separation and overriding of the articular facets take place. In like manner, when one of the lumbar disks is removed, the adjacent bodies tilt forward and separate posteriorly. At the lumbosacral area because of the angulation, size and position of the disk with its base or greatest thickness, in front and the narrowest in the back, the effect is more pronounced. Here, a narrowed disk produces a marked separation of the articular facets with resulting increase of the lumbosacral angle and flattening of the back. Thus, as the normal alinement of the lumbar vertebrae is changed, the normal physiologic relationship of the muscles and ligaments of the lower part of the back is disturbed. Muscle spasm and pain result. With a marked separation of the articular facets, such as occurs when the lumbosacral disk is involved, pathologic changes set in in the small joints, with stretching and distention of the joint capsule, often resulting in pressure on the fifth lumbar nerve root as it passes through the intervertebral foramen. Danforth and Wilson,<sup>4</sup> in a study of the lumbosacral region in relation to sciatic pain, found that the foramen between the fifth lumbar vertebra and the sacrum is always the smallest and the one between the fourth and the fifth lumbar vertebra the next larger. In contrast to the size of the foramen, the fifth lumbar nerve root is the largest and the fourth lumbar nerve root is next largest. Thus, when one considers that the fourth and fifth lumbar nerve roots are important parts of the lumbosacral plexus and that the largest nerve root passes through the smallest canal, the possibility of impingement of the nerve with resulting radiating pain down the limb becomes apparent.

#### ETIOLOGY

Degenerative changes of the disks are due mainly to the wear and tear of daily functional activity. The process is gradual and increases with age. When functional activity is moderate the disk undergoes only slight changes, and the spine may maintain its flexibility and mobility throughout life. When daily functional activity entails heavy physical labor marked degenerative changes of the disk develop. The disk becomes dry and firm loses its flexibility and becomes less adaptable and less resistant to the strain and stress of daily activity. This process

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<sup>4</sup> Danforth M. S. and Wilson P. D. The Anatomy of the Lumbo-Sacral Region in Relation to Sciatic Pain. *J. Bone & Joint Surg.* 7: 109 (Jan.) 1925.



Roentgenograms revealed a narrowed intervertebral disk between the second and the third lumbar vertebra, with evidence of herniation from the disk into the third lumbar body (fig 9). The normal lumbar lordosis was obliterated.

*Treatment*—A plaster of paris jacket was applied.

CASE 6—E. J., a white man aged 26, complained of pain in the lower part of the back. He gave a history of falling eight months before admission.

*Examination*—The lower part of the back was rigid. Motion of the spine was considerably restricted. Spasm of the sacrospinalis muscles was present. The double thigh flexion test gave positive results. Hyperextension of the spine gave rise to pain in the lumbosacral junction.

Roentgenograms revealed a narrowed lumbosacral intervertebral space.

*Treatment*—The spine was hyperextended, and a plaster of paris jacket was applied, holding the spine in slight lordosis.

CASE 8—S. V., a white woman aged 59, came to the clinic with a complaint of pain over the lower part of the back and of shooting pain down the back of both limbs. Pain was constant. The duration was four weeks and the onset was insidious.

*Examination*—The body was tilted to the left. Lumbar lordosis was considerably diminished despite the presence of a prominent abdomen. There was tenderness over the lumbosacral junction. Motion of the spine was not restricted.

Roentgenograms revealed osteoporosis of the spine and a marked compression and narrowing of the lumbosacral intervertebral disk, with sclerosis of the bony surfaces.

#### SUMMARY

Pathologic changes of the intervertebral disks are commonly observed at autopsy. The changes that take place vary from small herniations of the disk through vascular infiltration of the disk substance, fibrous replacement of the elastic tissue, brown degeneration, and finally shrinkage, narrowing and calcification of the entire disk. As a result, the disks lose their flexibility and resilience. They become firm, immobile and less resistant to the stress and shock of functional activity.

When a disk is narrowed anteriorly, the normal lumbar lordosis is diminished, and the articular facets are slightly separated. When the lumbosacral disk is narrowed the lumbosacral angle is increased, and there results a considerable separation of the articular facets. As a result of the malalignment of the facets arthritic changes take place, with consequent muscle spasm, pain and often impingement of the fifth lumbar nerve root resulting in sciatic pain down the leg.

Clinically the diagnosis of a narrowed intervertebral space is made from the roentgenograms, especially from the lateral and oblique views.

Seven cases in which there was roentgenographic evidence of a narrowed intervertebral space are reported, and the clinical course is reviewed. Pain in the lower part of the back was a constant complaint. In some cases there was associated sciatic pain down the leg. The treatment consisted in reestablishing the normal lumbar lordosis under general anesthesia and supporting the spine by means of a plaster of paris jacket.

articular facets and osteophytes around the margins of the bodies are usually associated and often result from a disturbance in the normal function of the disks. Subjective complaints and disabilities which these patients have are essentially an indication of a compromised and weakened spine.

In my series of cases of narrowed disks the main symptoms complained of were dull aching pains in the lower part of the back. Many of the patients had pain radiating down the backs of the lower limbs along the course of the sciatic nerve. The history of onset frequently given was of a slight injury, such as a slight fall, a sudden twist or the lifting of an object. Few were unable to recall any injury.

On examination the patients walked guardedly. The lower lumbar portion of the spine was held rigid and was often tilted to one side. Motion of the spine was restricted. Tenderness was present over the lumbosacral junction. There was often tenderness over the gluteal region, the area supplied by the superior gluteal nerve. Straight raising of the leg was limited when associated sciatic pain was present. Hyperextension of the spine gave rise to pain when the lumbosacral disk was involved.

#### ROENTGENOLOGIC OBSERVATIONS

Roentgenograms of the spine, particularly lateral and oblique views, established the diagnosis of narrowing of the disk. The intervertebral space was narrowed, and the lumbar portion of the spine was flattened. With the involvement of the lumbosacral disk, the lumbosacral angle was increased, and often a separation of the articular facets could be seen on the oblique views. Degenerative changes of the disks when associated with herniation of the disk into the vertebral bodies could be noted on the roentgenogram as small areas of lessened density surrounded by a sclerotic layer of bone. Calcifications of the nucleus pulposus were distinctly visualized.

#### TREATMENT

The treatment consisted in an attempt to reestablish the normal lumbar lordosis and to support the spine by means of a plaster of paris jacket. My aim was to realign the spinal structure to the normal or as near to the normal as possible and thus to relax the muscles and ligaments of the back. This might be accomplished by placing the patient on a convex frame or a padded plaster of paris bed for several weeks followed by an application of a plaster of paris jacket. I have obtained the best results by gently hyperextending the spine, while the patient was under general anesthesia until the normal lumbar lordosis was reached. A plaster of paris jacket was then applied from the upper part of the chest to the pelvis, holding the spine in the corrected position.

## INJURIES TO THE RETINAS AND OPTIC NERVES

As the eye constitutes an integral part of the central nervous system, injury to this organ must be given consideration. Retinal and preretinal hemorrhages, edema about the macula, commotio retinae and detachment of the retina should be mentioned. Such conditions may follow direct injury to the eyeball or occur secondarily as a result of trauma to the head. Hippocrates realized that amaurosis sometimes followed wounds inflicted on the eyebrows or calvarium. Retinal hemorrhages of various sorts may give rise to corresponding scotomas. Detachment of the retina is followed by varying forms of defects in the field. The visual disturbances secondary to commotio retinae or hemorrhage tend to clear

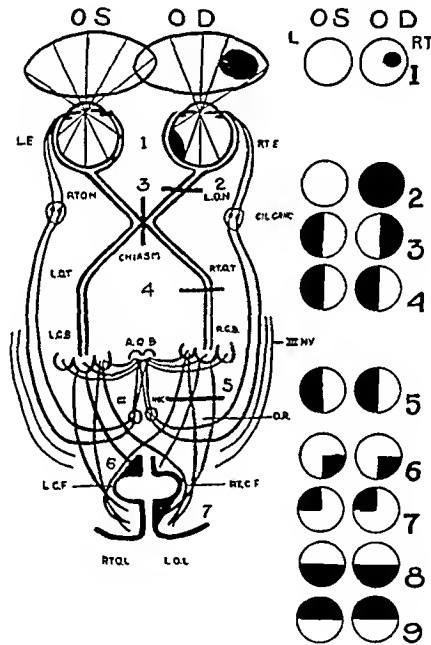


Fig 1—Diagrammatic representation of the visual pathways, with characteristic types of defects in the peripheral visual fields (after Gill<sup>2</sup>). (1) lesion of the retina in the nasal portion of the right eye with scotoma in the temporal field of the right eye, (2) lesion of the right optic nerve with complete loss of vision in the right eye, (3) lesion involving the optic chiasm, producing bitemporal hemianopia, (4) lesion involving the right optic tract with left homonymous hemianopia, (5) lesion involving the right optic radiations producing the same type of defect as that observed in (4), (6) lesion involving the anterior portion of the left calcarine fissure producing an inferior homonymous quadrantic anopsia, (7) lesion involving the posterior portion of the right calcarine fissure, producing a left superior homonymous quadrantanopia, (8) a combination lesion involving the anterior portion of both right and left calcarine fissures producing a bilateral inferior altitudinal hemianopia, (9) lesion of both posterior portions of the calcarine fissures, producing a bilateral inferior altitudinal hemianopia.

paris jacket extending from the upper ribs to the pelvis was then applied, holding the lumbar portion of the spine in lordosis

CASE 2—N H, a white man aged 46, was admitted to the hospital with a complaint of radiating pain down the backs of both legs and pain over the lower part of the back. He gave a history of having many similar attacks since 1917, each of which lasted several weeks

*Examination*—The patient was well developed. He walked guardedly, holding to objects for support. His body was tilted to the left. The spine was held rigid and flat. The lumbar curve was obliterated. Motion was restricted in all directions. There was spasm of the lumbar muscles. The straight leg-raising

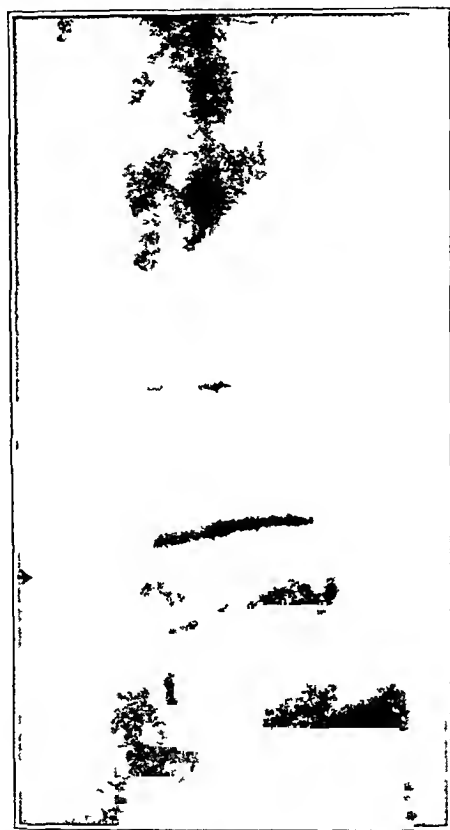


Fig 7 (case 2)—Lateral view, showing the narrowed fourth lumbar intervertebral space (marked by the arrow), with obliteration of the normal lumbar lordosis

test gave positive results on both sides. The double thigh flexion test gave negative results.

Anteroposterior, lateral and oblique roentgenograms revealed a distinct flattening of the intervertebral disk between the fourth and the fifth lumbar vertebra and slight anterior luxation of the fifth lumbar vertebra (fig 7).

*Treatment*—Under general anesthesia the lumbar portion of the spine was gradually hyperextended, reestablishing the normal lumbar lordosis. A plaster of paris jacket extending from the upper ribs to the pelvis was then applied, holding the lumbar portion of the spine in lordosis.

CASE 3—Y L, a white woman aged 35, came to the clinic with a complaint of pain over the left buttock and the lower part of the spine, with radiating pain

Smith<sup>7</sup> stated that von Holder found the walls of the orbit fractured seventy-three times in a series of eighty-six cases of fracture of the base of the skull. In the majority of cases the orbital fracture affected both the optic foramen and the optic canal. Under such circumstances one would expect that the optic nerve would be injured. Unless special attention is paid to this region, an orbital fracture is easily overlooked at postmortem examination. Such a fracture is frequently difficult to demonstrate in roentgen examination.

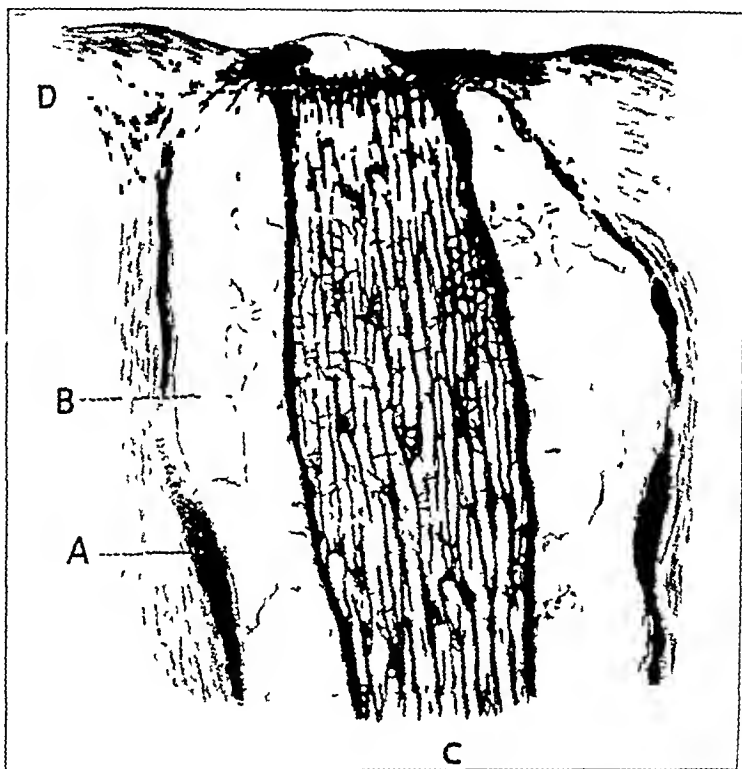


Fig 2—Drawing of microscopic section, showing *A*, a subdural hemorrhage in the intervaginal space, *B*, a distended subarachnoid space devoid of hemorrhage, *C*, marked compression of the optic nerve fibers, and *D*, moderate upward displacement of the lamina cribrosa. (After Cohen<sup>4</sup>)

Callan<sup>8</sup> reported four cases of orbital traumatism with immediate monocular blindness. He collected from the literature reports of eighty

7 Smith, A. E. Impairment of Vision Following Head Injury, *Minnesota Med* 14 809, (Sept) 1931.

8 Callan, P. A. Four Cases of Orbital Traumatism Resulting in Immediate Monocular Blindness Through Fracture into the Foramen Opticum, *J. A. M. A.* 18 284 (March 5) 1892.

the left leg. Left lumbar (sciatic) scoliosis was present. The lumbar portion of the spine was flat. Motion was restricted in all directions. A straight leg-raising test gave positive results on the left side. The double thigh flexion test gave negative results. Hyperextension of the spine gave rise to pain over the lumbosacral region.

Roentgenograms revealed that the fifth lumbosacral intervertebral space was narrowed and that the lumbar portion of the spine was flat. The lumbosacral angle was slightly increased.

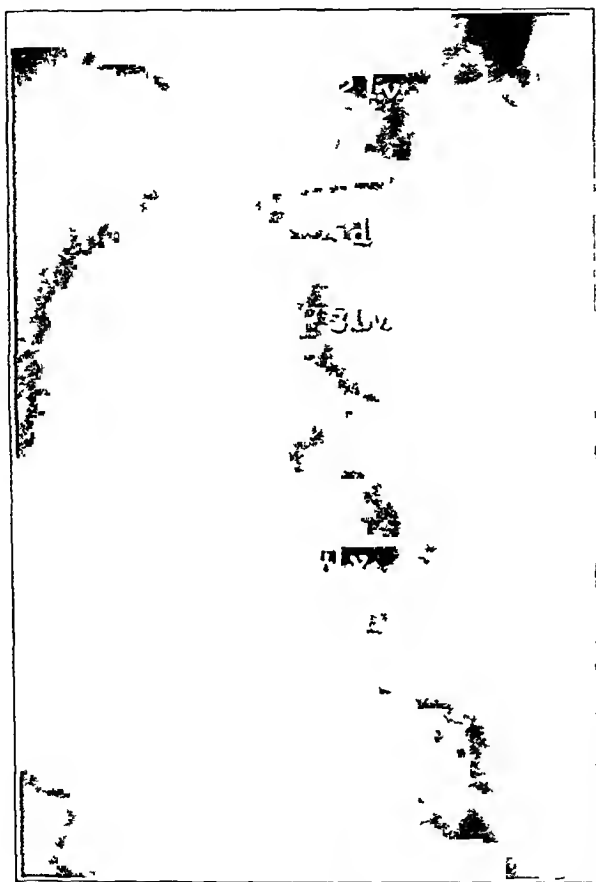


Fig 9 (case 5)—A narrowed intervertebral disk (1d) between the second and the third lumbar vertebra (1c). Note the semicircular area of lessened density indicative of a disk herniation at the upper margin and posterior third of the third lumbar vertebra (31c).

*Treatment*—The spine was hyperextended and a plaster of paris jacket was applied holding the lumbar portion of the spine in slight lordosis.

*CASE 5*—J Z, a white man aged 32, was admitted to the hospital with the chief complaint of pain over the lower part of the back of several years duration.

*Examination*—The patient was well developed and walked with a limp to the right. The dorsolumbar portion of the spine was held rigid. Tenderness was present over the second lumbar vertebra. The straight leg-raising test gave positive results.

cases of fracture into the optic foramen. He explained the mechanism of the fracture as follows:

The frontal bone unites with the nasal, submaxillary, lachrymal, and ethmoid bones by a continuous line of sutures, until the lesser wing of the sphenoid is reached, and at this point, the suture line bifurcates forming an obtuse angle, and quite near the apex of the angle is the foramen opticum. The jar made by the blow would find its weak point along this line of sutures, and the first resistance would be at the bifurcation adjacent to the foramen opticum. The movement or jar could not follow both lines with equal force at and beyond the bifurcation, consequently the unequal strain would result in fracture of the bone into the foramen opticum, causing compression of the optic nerve and sudden loss of vision in the eye.

Some writers have advocated decompression of the optic canal or exploration of the optic nerve in such cases of monocular blindness. The results of these attempts have been almost uniformly disappointing. Nothing can be expected if the nerve is crushed or severed, possibly better results may be obtained if it is infiltrated by blood or moderately compressed, as the sheath can be opened and pressure on the nerve relieved.

Plum<sup>9</sup> advised immediate operation when a fracture through the optic foramen results in monocular blindness.

Eagleton<sup>10</sup> stated: "Very slight pressure on the nerve itself as it passes through the bony optic foramen may cause loss of sight, which, if not early recognized and surgically relieved, will rapidly result in permanent blindness." I have not explored the optic nerve under these conditions. Perhaps such exploration should be recommended. While usually carrying little risk, such a procedure may occasionally be hazardous, as the following case indicates. A man aged 29 sustained multiple fractures of the left orbit, easily demonstrated roentgenologically. No fragments were displaced. Immediate ophthalmoplegia and monocular blindness resulted. Aside from these complications the patient apparently made an uneventful recovery. Two months later sudden fatal hemorrhage from the left nostril ensued. Autopsy revealed a healed fracture of the left orbital plate and frontal bone with recent erosion of the wall of the left cavernous sinus. At no time was a murmur present. The fatal hemorrhage might have occurred at operation.

#### INJURIES TO THE OPTIC CHIASM

From the standpoint of their mechanical production injuries to the optic chiasm are highly interesting. The mechanism of their production

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9 Plum, F. A. Ophthalmological Symptoms Associated with Intracranial Injuries, *West J Surg* **39** 754 (Oct.) 1931.

10 Eagleton, W. P. Traumatic and Infective Lesions of the Head, the Chief Manifestations of Which Are Visual Disturbances. Their Diagnosis and Surgical Treatment, *S Clin North America* **68** 1435 (Dec.) 1926.

# ALTERATIONS IN THE VISUAL FIELDS FOLLOWING CRANIOCEREBRAL INJURIES

CARL WHEELER RAND M D

LOS ANGELES

During the past decade injuries to the brain have been analyzed in greater detail than ever before. The recognition of localizing signs and symptoms consequent to these injuries from the standpoint both of prognosis and of treatment is of great importance. For example in a group of cases of injury to the head the cranial nerves may be studied collectively or one's attention may be profitably limited to the study of a single nerve and its intracranial ramifications. The following observations are confined to injuries of the optic nerves and their pathways as revealed by alterations in the visual fields.

Loss of vision a serious complication following head injuries fortunately is not frequent. Phelps<sup>1</sup> found injury to the optic nerves six times in two hundred and forty-five cases of fractures of the base of the skull (2.4 per cent). This relative infrequency is surprising when one considers the extensive ramifications of the entire visual mechanism and bears in mind the great variety of methods by which craniocerebral injuries are produced. Somberg<sup>2</sup> pointed out that a patient may overlook moderate visual defects because of the overlapping of the binocular fields. While the types of visual defects following injury to the visual pathways are many they may be accurately outlined. In discussing them it is necessary to consider traumatic lesions occurring along the visual pathways from the retinas to the tips of the occipital lobes (fig. 1). Organic lesions tend to leave permanent visual defects. Changes in the fields due to hysteria on the other hand being functional are usually less permanent. The latter however probably constitute the larger group. In such cases for fear of fixing the neurosis it is unwise to place undue emphasis on the visual defect by repeated examinations. In this presentation alterations in the fields resulting from organic rather than from functional conditions will be given primary consideration.

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1 Phelps Charles. *Traumatic Injuries of the Brain and Its Membranes*. New York: D. Appleton & Company, 1897, p. 25.

2 Somberg J. S. *Traumatic Lesions of the Optic Pathways with Report of a Case*. *Am. J. Ophth.* 10: 115 (Feb.) 1927.





Fig 5—Longitudinal splitting of the chiasm with cross-tearing of one optic nerve following a fracture of the base of the skull. This type of lesion may be produced by traction on one optic nerve, causing total blindness in one eye and temporal hemianopia in the opposite visual field. (After Liebrecht<sup>5</sup>)



Fig 6—Anteroposterior separation of the commissure shown experimentally on the cadaver. When the glabella is widely spread the optic nerves separate, producing anteroposterior splitting of the chiasm. This is not tenable clinically. (After Coppez<sup>13</sup>)

up, those consequent to detachment of the retina are permanent unless they are surgically corrected

Rarely, a transient choking of the disks, for which no plausible explanation is at hand, may follow a head injury. During its presence one finds lowering of the acuity of vision, general contraction of the visual fields and enlargement of the blindspots such as occur in cases of papilledema secondary to tumor of the brain. The fields improve as the choking subsides. Most frequently choking of the disks accompanies chronic subdural hematoma, abscess of the brain or pneumocephalus. If the lesion brings pressure to bear on the visual pathways, defects in the fields occur, and they become permanent unless the cause is removed.

Gill<sup>3</sup> stated that loss of vision following hemorrhage into the orbit is slowly, rather than suddenly, progressive. Hemorrhage under the sheath of an optic nerve, frequently associated with fracture of the orbit impairs or destroys vision. As this sheath is a prolongation of the dura, subdural or subarachnoid hemorrhages may find their way beneath it (fig 2, Cohen<sup>4</sup>), causing pressure on the visual fibers (fig 3, Liebrecht<sup>5</sup>). Again, rupture of the central artery or vein (fig 4) or acute angulation at their point of emergence from the nerve is said to cause blindness.

Commonly, injury to the optic nerves follows a gunshot wound of the head. One frequently finds a person blinded in one or in both eyes as a result of having the optic nerves severed by a bullet. Orbital fractures, especially those involving the optic foramen, cause monocular, rarely binocular, blindness. Miceli<sup>6</sup> reported the instance of a patient with a fracture involving the right optic canal who subsequently died of pneumonia. Postmortem examination showed the optic nerve to be thickened in a clublike manner, the greater swelling being toward the anterior extremity. Microscopically the intervaginal space was increased, the increase being more marked distally. The nerve fibers in the lamina cribrosa were tightly packed, small vacuoles of varying size being interposed between the tracts. Ovoid lacunae, some of which penetrated the distal sheath, were present on the arachnoid side.

3 Gill, W. D. Eye Symptoms in Head Injuries, *M. Rec. & Ann.* **25** 676 (Feb.) 1931.

4 Cohen, Martin. The Value of Eye Manifestations Complicating Fractured Skull. Preliminary Report, *Arch. Ophth.* **46** 258 (May) 1917.

5 Liebrecht. Schadelbruch und Auge, *Arch. f. Augenh.* (J. F. Bergman, Munich) **55** 36, 1906, Schadelbruch und Sehnerv, *Arch. f. Ophth.* **83** 525, 1912.

6 Miceli, I. Alterations in Optic Nerve Following Injuries to Head, *Gior. di ocul.* **6** 45, 1925.

The hydrodynamic force of a displaced third ventricle must be given consideration. I have seen two cases (cases 6 and 9) in which the chiasmal lesion followed a depressed fracture of the vault. The force was applied above and must have been transmitted directly to the chiasmal region with something of a contre-coup effect. At least, the chiasm must have been forced against the underlying sella. In addition, injury to the infundibulum may occur concurrently, with resultant symptoms of diabetes insipidus. Splinters of bone projecting from the floor of the skull and causing direct injury to the chiasm are so rare that they need not be given serious consideration.



Fig 7—Transverse tearing of both optic nerves at the chiasm produced in the cadaver by wide separation of the skull in the petrosphenoid region. Such lesions do not occur clinically. (After Coppez<sup>13</sup>)

#### INJURIES TO THE OPTIC TRACTS

After the World War, abundant human material was provided for studying the cortical visual centers and their associated tracts. Particularly was this true in cases of gunshot wounds of the occipital lobes, in which both the position of the missile and its tract were known. Extensive observations were made by Fleischer and Ensinger,<sup>16</sup> Beau-

<sup>16</sup> Fleischer, B., and Ensinger, T. Homonymhemianopische Gesichtsfeldstörungen nach Schädelspez Hinterhauptschüssen, *Klin Monatsbl f Augenh* 65: 181, 1920.

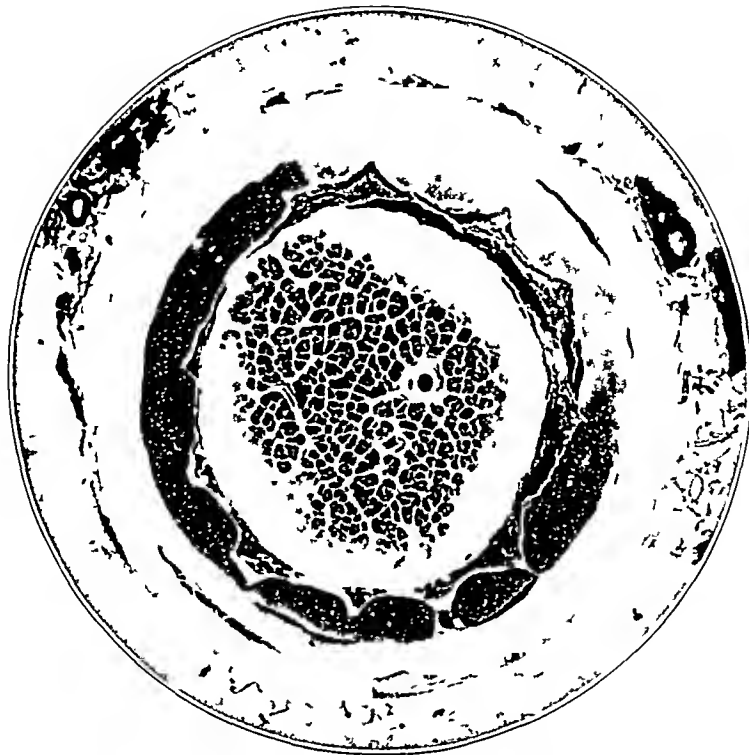


Fig 3—Cross-section of an optic nerve particularly showing bleeding into the subdural space The subarachnoid space is dilated by lymph and some bleeding (After Liebrecht <sup>5</sup>)



Fig 4—Diagrammatic representation of an optic nerve showing bleeding from the central vein The vaginal space is widely dilated by lymph and blood Detachment of the retina was present (After Liebrecht <sup>7</sup>)

certain disturbances of the higher visual perceptual functions with intact visual sensibility, as loss of visual orientation and localization in space, disturbance of the perception of depth and distance, visual attention loss, and visual agnosia

### Scarlett and Ingham<sup>20</sup> concluded

- 1 Fixation of vision and normal visual acuity are commonly retained when lesions of the occipital lobes have caused a complete homonymous hemianopia (When both occipital lobes were injured, visual acuity was reduced in both eyes. No disturbance of fixation was demonstrated even in these cases)
- 2 The hemianopic fields commonly approached to within a fraction of 1 degree of the fixation point
- 3 Evidence that macular vision is represented in the apex of the occipital lobe is furnished
- 4 Defects of the visual fields, scotomas or hemianopias, resulting from lesions of the occipital lobes, are roughly symmetrical but not exactly superimposable
- 5 Greatly reduced visual perception in homonymous fields (incomplete hemianopia) may exist as a permanent residual result of occipital injury. In such cases bright lights and large moving objects can be discerned in fields which are blind to the usual tests for form and color

Ingham and Lyster<sup>24</sup> reported the case of a patient who was under my observation at the Los Angeles County Hospital. This patient, a man aged 27, had sustained a gunshot wound in the occipital region, having been shot from behind while driving his automobile. He experienced a flash of light followed by momentary blindness. Vision quickly returned, however, he could only see above the horizontal plane but not below it. He could not see the road and turned the wheel over to his wife. He was not unconscious at any time. On his admission to the hospital a gunshot wound was found rather high in the midoccipital region. A depressed fracture was present and the bullet was flattened near the junction of the lambdoid and the sagittal suture (fig 8). Dr. Eliot Alden removed the bullet with the depressed fragment of bone and found the dura to be intact. This patient presented a typical bilateral inferior hemianopia on rough tests. The fields above the horizontal plane were normal. Central vision was good. Small test objects were not recognized in the lower half of either visual field until they approached the horizontal plane. Large objects could be seen 40 degrees below the fixation point. The two fields were symmetrically affected. The case illustrated the following points emphasized by Ingham and Lyster: "(1) the subjective flash of light perceived at the instant of the injury to the occipital cortex, (2) symmetrical horizontal inferior hemianopia resulting from a presumably superficial lesion of both occipital lobes close to the midline about 6 cm from the apexes of

<sup>24</sup> Ingham S. D. and Lyster T. C. Abnormalities of the Visual Fields, J. A. M. A. 82:17 (Jan 5) 1924

has not been satisfactorily explained. As there is great variation in the relation of the chiasm to its surrounding structures, certain anatomic factors must be borne in mind. Walker,<sup>11</sup> in citing the work of Schaeffer, stated

the chiasm was found to fit in close relationship with the chiasmal sulcus in only five per cent of the cases, while in four per cent the chiasm was located entirely behind the diaphragm, resting on the posterior sella. In twelve per cent the chiasm covered the central portion of the diaphragm, while in seventy-nine per cent the chiasm covered only the posterior half of the diaphragm, with the posterior part of the chiasm projecting variously over the dorsum sellae.

One must also bear in mind the wide variation existing in the size and shape of the sella turcica, with especial reference to variability in the prominence of the clinoid processes. Naffziger<sup>12</sup> mentioned an instance in which total blindness followed a fall from a hay wagon, resulting in dislocation of a long-standing pituitary tumor which had previously caused insignificant symptoms. He also cited an instance in which after a fracture of the anterior fossa and squamous portion of the right temporal bone monocular blindness developed on the third day. Death occurred two weeks later, resulting from pneumonia. Naffziger stated "Autopsy revealed a displacement of the right anterior clinoid downward compressing the nerve to a flattened ribbon of about one third its normal thickness. In front of the compressed portion the nerve and its envelope were very bulbous and edematous."

When injured, the chiasm is frequently split in an anteroposterior direction, as represented by Liebrecht.<sup>5</sup> In his illustration, besides the sagittal tearing of the chiasm a transverse, almost complete, laceration of the left optic nerve is shown (fig. 5). Such lesions can be produced experimentally (fig. 6).

Recently Coppez<sup>13</sup> reported three cases of bitemporal hemianopia and panoramic scotoma. He attempted to explain the mechanism of these chiasmatic syndromes. He believed that the injury may occur in one of three ways

1. As a result of a violent injury of the frontal region, which increases the transverse diameter of the skull. In discussing such lesions Coppez referred to the proposition of Liebrecht.<sup>5</sup> Felizet<sup>14</sup> had already shown that this diameter could be increased as much as

11 Walker, C. B. Lesions of the Chiasmal Region, *Am. J. Ophth.* **13** 198 (March) 1930.

12 Naffziger, H. C. Certain Eye and Ear Affections in Association with Head Injuries, *Ophth. Rec.* **25** 502, (Oct.) 1916.

13 Coppez, Henri. Le mecanisme des lesions du chiasma dans les fractures du crane, *Arch. d'ophth.* (Masson & Cie, Paris) **46** 705 (Dec.) 1929.

14 Felizet, G. M. Recherches anatomiques et experimentales sur les fractures du crane, Paris, A. Delahayer, 1873.

the patient could see moving objects, and by the next morning he had completely regained his vision. It was concluded that the injury was a localized cerebral concussion due to contre-coup violence affecting the visual centers of both occipital lobes. Newmark<sup>27</sup> reported the case of a 21 year old prize fighter who was struck on the jaw and fell on the back of his head. No fracture of the skull was demonstrated, but right hemianopia and astereognosis developed and a Babinski sign appeared bilaterally. Hearing was impaired on the right side. Seven days later the patient seemed completely blind but persisted in saying that he could see. Three weeks later he could see moving objects, and six weeks later he could count fingers. Visual aphasia developed, the patient being unable to name colors, although he could collect colors and match them. Ultimately the central vision became good, although the fields remained contracted. It was the impression that in cases of softening of both occipital lobes temporary amaurosis is more common than permanent blindness, and in cases of visual aphasia the patient may be unconscious of his blindness. In some cases one would suspect that in a minute circle around the fixation point there remained sensibility to light. A functional element in this case was suspected. I recently observed a case of an almost identical condition in which vision was regained within forty-eight hours.

Newmark<sup>27</sup> cited the case of a 4 year old boy who was struck by an automobile and in whom a hematoma of the occiput developed. He remained unconscious for three days. There was a linear fracture of the occipital bone. When the patient regained consciousness, he was blind. There was no return of vision for six months, then central vision appeared and seemed good. The fields were narrow. Two years later the fields were markedly contracted, and the fundi, which at first were said to be normal, showed pallor of the optic disks, the right disk being more affected than the left. Newmark also referred to a case of Hirsch,<sup>28</sup> that of a 12 year old boy who sustained a blow between the lambda and the external occipital protuberance. No fracture resulted. There was immediate complete amaurosis. All sensibility to light was absent, although the pupils reacted sluggishly to light and the fundi remained normal. Three hours later the child could perceive large white objects, seven hours later he could count fingers. Right homonymous hemianopia with normal pupillary reactions appeared. Two days later the fields and the visual acuity were normal. Although

<sup>27</sup> Newmark, L. Blindness Following Injuries to the Back of the Head. *California State J M* **12** 183 (May) 1914, **14** 487 (Dec) 1916.

<sup>28</sup> Hirsch, C. Ueber passagere Rindenblindheit durch Commotio cerebri. *Deutsche med Wchnschr* **36** 1436 1910.

8 mm without actual fracture occurring. In order to cause fracture, greater violence is necessary. If sufficient force is used to fracture the ethmoid region in an anteroposterior direction the distance between the optic canals will be increased and consequent spreading of the chiasm will occur. If the chiasm is completely split bitemporal hemianopia will result. If some of the bundles of crossed fibers are spared, islands of vision will remain in the temporal fields. Coppez<sup>13</sup> reproduced these lesions experimentally on fresh cadavers. He stated that if the disjunction was increased until the nerve spread reached 26 mm, the anteroposterior rent of the chiasm was complete. He added that the nerves being held tightly by the dural sheath always remain in the optic canal. He admitted that it is difficult to believe that this could happen during life (fig 6).

2 As a result of anterolateral fracture with destruction of the external walls of the orbit extending to the sphenoid and the optic canal. According to Coppez, fracture of this type is observed in cases in which the head is crushed by the wheel of an automobile or carriage. The contents of the orbit are badly injected and pushed forward. This produces avulsion of the globe and stretching of the optic nerve. The latter ruptures at the anterior orifice of the optic canal if the attachment of the nerve to the canal remains fast. If, on the other hand, the canal is fractured the nerve is loosened and tears at the level of the chiasm. This demonstrates that the chiasm is more fragile than the optic nerve. Traction on the nerve results not in rupture of the nerve trunk but rather in avulsion at the level of the chiasm. Coppez<sup>13</sup> reproduced this type of lesion experimentally by pulling out an eyeball with its attached nerve after freeing the adhesions in the optic canal. Under these circumstances the chiasm is torn transversely.

3 As a result of fracture of the petro-occipital junction directed toward the sphenopetrosal junction. According to Coppez such fractures were studied, especially by Bollack<sup>15</sup> from the standpoint of the chiasmatic syndrome. The fracture tends to run parallel to the axis of the petrous bone, often reaching the sella turcica from behind forward and from the lateral toward the mesial border. It is perpendicular to the optic nerve on the same side. One must assume that the optic nerve is violently stretched by separation of the bone. This separation occurs in the direction of the nerve. It may be assumed that the nerve is violently pulled by the spread of the bone, the force then being transmitted to the chiasmal fibers which are torn transversely (fig 7). Clinical examination tends to support this view in cases of fracture of the petro-occipital or the sphenopetrosal bones.

15 Bollack cited by Coppez<sup>13</sup>



questionable. He mentioned cases cited by Binet and Janet, as quoted by de Schweinitz, of patients suffering from hysterical blindness who have been hypnotized. When the hypnotic state was induced such patients could recall what they saw during the period of alleged amaurosis. This experience is used as an argument tending to support the theory of integrity of the sensory end-organs.

Many analogies may be drawn both from the general sensory patterns and from the alterations in the visual fields produced by hysteria. Anesthesia and hyperesthesia of the skin find their counterpart in the retina, as shown by amblyopia, amaurosis or scotomas. These may be bilateral or unilateral. Peter stated "It is well to emphasize the fact that no part of the visual pathway enjoys immunity in hysteria, and that any variation of the field observed in organic disease of the visual tract may be found in hysteric disease." Three types of changes in the fields are especially characteristic: (1) Concentric contraction of fields, with or without central amblyopia, (2) tubular fields, (3) reversal of color fields. Concentric contraction most frequently is of circular shape, and the field may be limited almost to the center of vision. Usually the fields for form and color are almost equal in size. The fields for color on the other hand, may be contracted in their usual order proportionately to the reduction in the fields for form, as seen in cases of optic neuritis. The eyegrounds, of course are normal. Tubular fields leave no doubt as to the diagnosis of hysteria. Ordinarily, as the distance between the patient's eye and the screen is increased, the contracted field enlarges, in cases of tubular vision a field of the same size may be obtained at any distance. This is said to occur in cases of malingering as well as in cases of hysteria. Reversal of the fields for color and interlacing especially in conjunction with concentric contraction or tubular vision, is characteristic of hysteria. Various types of oculomotor palsy may occur in cases of hysteria. Photophobia may likewise occur, probably expressing any analogy to hyperesthesias of the skin as shown in this condition.

#### REPORT OF CASES

CASE 1—*Rupture of the left eyeball paracentral scotoma of the right visual field following a blow across the bridge of the nose. Commotio retinac (?)*

J F J, a man aged 22 married a truck driver, was referred by Dr John D Gillis on March 24, 1931. The patient was injured on March 23, 1931, when a tire rim sprang back striking him across the bridge of the nose and the forehead. He was momentarily dazed. He sustained a laceration 8 cm long across the forehead and the bridge of the nose, a fracture of the frontal sinus and a rupture of the left eyeball. On the following day Dr J M Osburn removed the eyeball.

*Resume of Complaints and Findings*—On July 24 there were headache, dizziness complete loss of smell, pain in the right eye and right side of the face and

vieux,<sup>17</sup> Holmes and Lister,<sup>18</sup> Holmes,<sup>19</sup> Scarlett and Ingham<sup>20</sup> and many other authors.<sup>21</sup> Studies by Fox and German<sup>22</sup> and by Penfield, Evans and MacMillan<sup>23</sup> following complete or partial lobectomies of the temporal or occipital lobe afforded excellent opportunities for perimetric observations which had been anatomically and physiologically controlled.

Holmes<sup>19</sup> summarized his conclusions as follows:

- 1 The upper half of each retina is represented in the dorsal, and the lower in the ventral part of each visual area.
- 2 The centre for macular or central vision lies in the most posterior part of the visual areas, probably on the margins, and in the lateral surfaces of the occipital poles. The macula has not a bilateral representation.
- 3 The centre for vision subserved by the periphery of the retinae is situated in the anterior portions of the visual areas, and the serial concentric zones of the retinae from the macula to the periphery are probably represented in this order from behind forwards in the visual areas.
- 4 Those portions of the retinae adjoining their vertical axes are probably represented in dorsal and ventral margins of the visual areas, while that in the neighborhood of the horizontal axes is projected onto the walls and the floor of the calcarine fissures.
- 5 Severe lesions of the visual cortex produce complete blindness in the corresponding portions of the visual fields, or, if incomplete, an amblyopia, color vision being lost, and white objects appearing indistinct or only more potent stimuli, such as objects moved sharply, may excite sensations.
- 6 The defects of vision in the fields of the two eyes are always congruous and superimposable provided that no disease or injury of the peripheral visual apparatus exists.
- 7 Lesions of the lateral surfaces of the hemispheres, particularly of the posterior parietal regions may cause

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17 Beauvieux. Les troubles visuels dans les blessures par coup de feu de la sphere visuelle corticale ou des radiations optiques, *Arch d'opht* **35** 410, 458, 560 and 617, 1916-1917

18 Holmes, G, and Lister, W T. Disturbances of Vision from Cerebral Lesions, with Special Reference to the Cortical Representation of the Macula, *Brain* **39** 34 (June) 1916

19 Holmes, G. Disturbances of Vision by Cerebral Lesions, *Med Press Circ* **104** 490 (Dec 26) 1917

20 Scarlett, H W, and Ingham, S D. Visual Defects Caused by Occipital Lobe Lesions, *Arch Neurol & Psychiat* **8** 225 (Sept) 1922

21 Meyer, A. The Connections of the Occipital Lobes and the Present Status of the Cerebral Visual Affections, *Tr A Am Physicians* **22** 7, 1907. Allen, I M. A Clinical Study of Tumors Involving the Occipital Lobe, *Brain* **53** 194, 1930. Horrax, G, and Putnam, T. The Field Defects and Hallucinations Produced by Tumors of the Occipital Lobe, *ibid* **55** 499, 1932. Traquair, H M. Fields of Vision in Intracranial Lesions, *Brit M J* **2** 229, 1933. Brouwer, B. Projection of the Retina on the Cortex in Man, *A Research Nerv & Ment Dis, Proc* **13** 529, 1934

22 Fox, J C, Jr, and German, W J. Observations Following Left (Dominant) Temporal Lobectomy, *Arch Neurol & Psychiat* **33** 791 (April) 1935

23 Penfield, Wilder, Evans, J P, and MacMillan, J A. Visual Pathways in Man with Particular Reference to Macular Representation, *Arch Neurol & Psychiat* **33** 816 (April) 1935

## ARCHIVES OF SURGERY

*Resume of Complaints and Findings*—When the patient recovered consciousness he complained of complete blindness in the left eye. This eye was edematous and ecchymotic, and the pupil was enlarged. The results of ophthalmic examination were negative shortly after the accident but later primary atrophy of the optic nerve developed on the left side. The patient suffered from the usual post-traumatic headache and dizziness. He began to recover vision in the left eye at the end of a month. Vision improved slowly but steadily.

Dr Clifford B Walker, ophthalmologist, on studying the patient's eyes on Oct 10, 1933, found a normal field on the right side, on the left side there were loss of vision except for the lower nasal quadrant (fig 10) and advanced primary atrophy of the optic nerve.

Roentgenograms of the optic foramina showed slight fracture of the left sphenoid wing, with slight narrowing of the left foramen.

*Impression*—Concussion and fracture of the skull involving the left optic foramen were considered to be present. The defect in the left visual field was probably caused by direct injury to the optic nerve at the foramen.

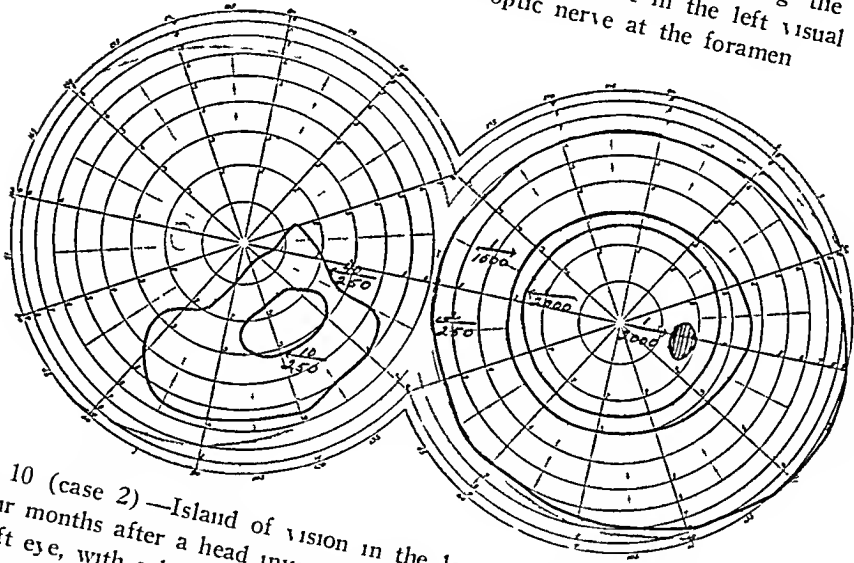


Fig 10 (case 2)—Island of vision in the lower temporal portion of the left field, four months after a head injury. There was immediate monocular blindness in the left eye, with subsequent recovery of vision. Primary atrophy of the optic nerve occurred. The nerve was injured near the optic foramen. Corrected vision was 3/200 in the left and 20/15+ in the right eye.

CASE 3—Left visual field preserved only in the upper nasal quadrant, right visual field normal. Primary atrophy of the optic nerve on the left, moderate atrophy on the right.

O R W, a man aged 20, single, a miner, was referred by the State Compensation Insurance Fund on July 2, 1934. He was injured on May 23, 1934, in a tunnel cave-in. He had no recollection of the accident, he recovered consciousness the following day but was irrational for several days.

*Resume of Complaints and Findings*—There were headache, dizziness, backache and loss of vision in the left eye. Both disks were clearly outlined and of normal color and showed unusually large cups. The pupils were equal and reacted well to light and in accommodation. There were numbness of the right side of the face and partial peripheral paralysis on the right side. On July 12,

the lobes, and (3) absence of the common general symptom of cerebral concussion" The patient left the hospital before perimetric studies could be made

#### TEMPORARY BLINDNESS FOLLOWING CONCUSSION

Instances of temporary blindness following injury to the back of the head may be cited Baldwin<sup>25</sup> reported a case of a patient who sustained a gunshot wound of the right occipital region, the bullet passing to the left occipital lobe At operation the right occipital lobe showed wide disorganization of brain tissue with hemorrhage, a piece of bone being extracted from the left occipital lobe The bullet was not removed Immediately after the injury the patient was totally blind and the pupils were dilated and fixed Three days later he began to see slightly, the pupils were small and responded to light Two months

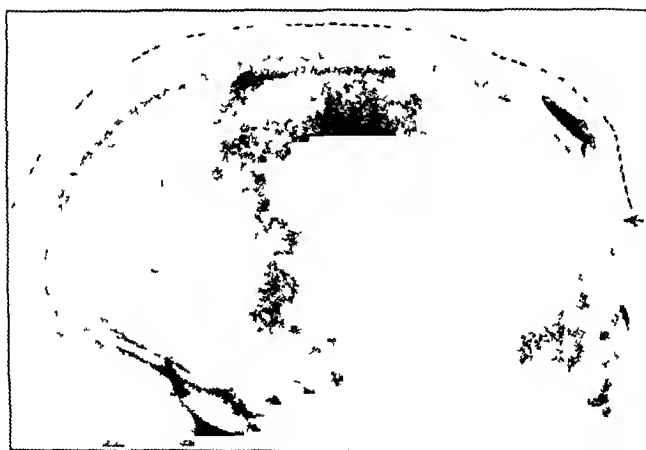


Fig 8—Depressed occipital fracture with a flattened bullet in the upper part of the occipital region Lower homonymous hemianopia resulted (After Ingham and Lyster<sup>24</sup>)

later vision returned in the right upper homonymous quadrant, and six months later there was homonymous hemianopia, with normal acuity and no changes in the fundi Anderton<sup>26</sup> reported the case of a 9 year old child who was kicked in the forehead by a horse He remained completely conscious but became totally blind, not even having perception of bright light The pupils remained equal and reacted quickly Two hours later perception of light returned, four hours thereafter

25 Baldwin, H C Brain Injuries 1 Gunshot Wound Involving Both Occipital Lobes Study of Visual Fields 2 Fracture of Skull Injury to Frontal Lobe Boston M & S J 154 185, 1906

26 Anderton, G Temporary Blindness After Concussion Brit M J 2 1005 (Nov 28) 1925

margins of the disk were sharply cut and pale, there was primary atrophy of the optic nerve, the veins were of moderate size, the arteries were small, there were no hemorrhages, exudates or elevation. There was complete paralysis of both external rectus muscles. Apparently the right oculomotor nerve was not involved, on the left side there was partial ptosis. The right pupil reacted readily to light directly but not consensually, the left pupil reacted to light consensually but not directly. The patient was unable to turn the left eye out and up, but he could turn it down and in. On the right side the ocular movements were essentially normal except that the patient could not turn the eye out. The trochlear nerve had apparently escaped injury on the right, but was partially involved on the left. There was complete blindness in the left eye, vision was good in the right. The blood pressure was 125 systolic and 80 diastolic. Examination on Feb 4, 1935, showed advanced primary atrophy of the optic nerve on the left side, the disk being pearly white and the arteries threadlike. On

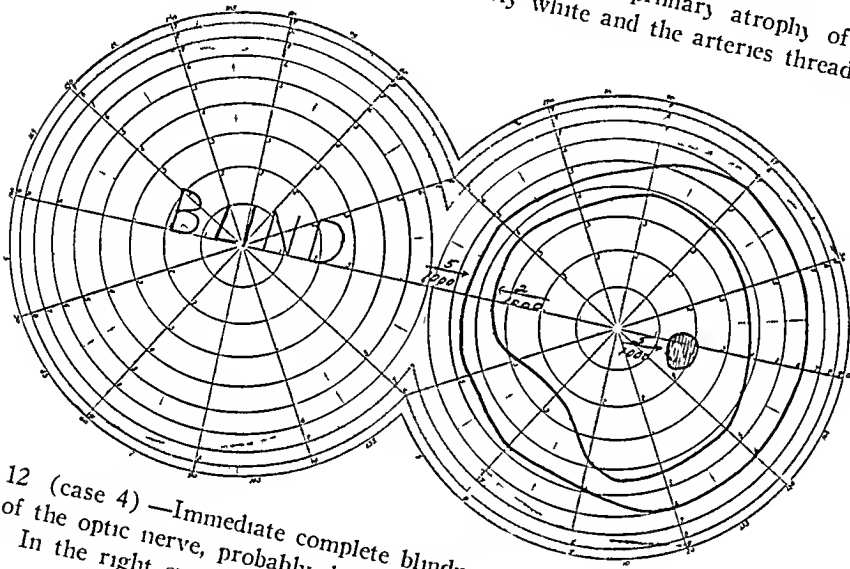


Fig 12 (case 4) — Immediate complete blindness in the left eye, with primary atrophy of the optic nerve, probably due to injury of the optic nerve at the optic foramen. In the right eye uncorrected vision was 20/40, corrected vision, 20/30.

the right side the disk was sharply outlined, the optic cup was distinct, the veins were of good caliber, the arteries were small and the disk was somewhat paler than normal. The pupils were unequal, the left pupil being larger than the right. The left pupil did not react to light but reacted consensually. The right pupil reacted quickly to direct light but did not react consensually. Hypesthesia to touch over the entire distribution of the left trigeminal nerve and corneal anesthesia persisted. Hearing was diminished on the right side. Weber's test showed the sound referred to the right. Determination of the visual fields showed complete blindness on the left and an approximately normal field on the right side (fig 12). Roentgenograms of the skull showed a linear fracture in the right temporal region.

*Impression* — The disturbances were regarded as being due to injury to the left optic nerve at the optic foramen, resulting in monocular blindness and primary atrophy of the optic nerve. There was involvement of other cranial nerves.

transient blindness occurred, the hemianopia was considered hysterical. Hirsch expressed the belief that "the visual centers in both occipital lobes had been affected, the right hemianopia remaining for a while after the right occipital cortex had recovered." I agree with Newmark in assuming that a commotio cerebri was present, for the restoration of vision was more rapid than would have been the case if a hemorrhage had occurred.

Word or mind blindness does not occur as frequently as one might expect. Gibson<sup>29</sup> reported a case of a through and through gunshot wound of the head with almost total destruction of the primary visual cortex to the mesial aspect of the left occipital lobe specially involving the calcarine fissure and cuneus and causing some injury to the visual cortex of the right side. Right homonymous hemianopia developed. The fundi were normal. The patient apparently had visual agnosia. He did not know the nature of most objects, although he avoided them. Some were recognized imperfectly. By the aid of his eyes he could pick up comparatively small objects from the floor, but he did not know what they were until he felt them. He did not know his wife when he met her on the street, nor could he tell a man from a woman by sight. He had attacks of complete blindness, sometimes lasting for a day, these were thought to be epileptic. Gibson concluded:

The images formed on each retina are no doubt perfect and the messages from the retina are carried to the visual cortex, but they are not received by the practically destroyed left primary visual cortex and are imperfectly recognized by the injured right primary visual cortex. He is word-blind, letter-blind and partly object-blind. The right visual cortex in right handed people does not recognize word pictures and perhaps not letter pictures, but it apparently recognizes objects as such except when injured as in this man.

#### ALTERATIONS IN THE FIELDS DUE TO HYSTERIA

It is not my purpose to discuss in detail the various alterations in the fields due to hysteria following head injuries. In my experience, they are more commonly met with than alterations having a true organic background. This is not strange when one remembers the diversity of symptoms of hysteria which occur after industrial injuries. Peter<sup>30</sup> regarded the changes in the visual fields shown in hysteria as being due to inhibition or loss of will power on the part of the patient. This results in the patient's not responding normally to usual stimuli. Whether this is due to failure of the retinal sense organs in receiving impressions or to failure of the central end-organs to stimulate consciousness is

<sup>29</sup> Gibson, J. L. Bullet Wound Injury to Visual Cortex on Each Side, *M. J. Australia* 1: 86 (Jan. 24) 1925.

<sup>30</sup> Peter, L. C. *The Principles and Practice of Perimetry*, Philadelphia, Lea & Febiger, 1931, p. 265.

## ARCHIVES OF SURGERY

Determination of the visual fields made on Jan 25, 1935, showed complete blindness in the left eye and moderate contraction of the upper temporal portion of the field on the right side (fig 13)

*Impression*—The disturbances were considered to be due to a gunshot wound of the head, resulting in severance of the left optic nerve by a bullet

CASE 6—*Blindness in the left eye, temporal hemianopia on the right side following a blow on the head Bilateral primary atrophy of the optic nerve*

E S, a man aged 26, a rotary helper, was referred by the State Compensation Insurance Fund on Dec 14, 1928. He was injured on Oct 13, 1928, when he was struck on the top of the head by a falling elevator link. He sustained an extensive compound comminuted depressed fracture of the skull. Operation was performed soon after by Dr Robert W Wilcox, of Long Beach, Calif. The brain was found to be lacerated. Convalescence was slow.

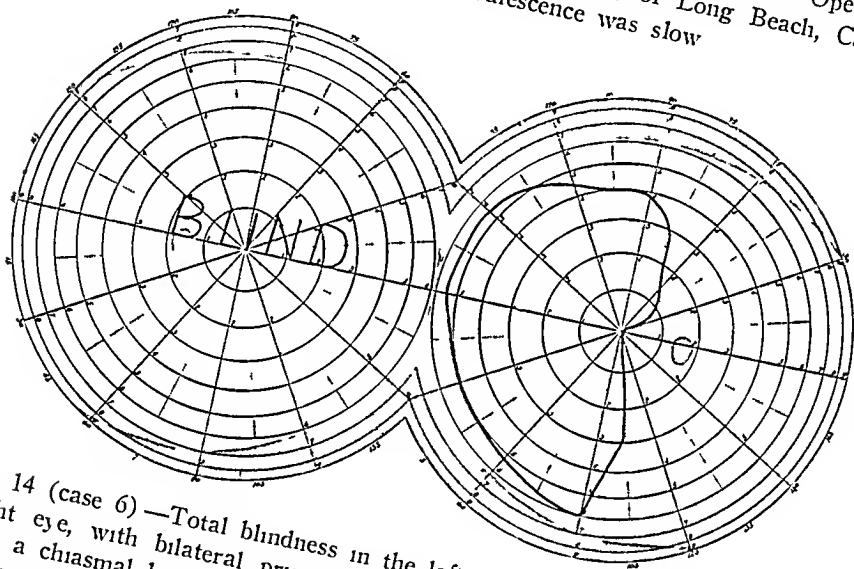


Fig 14 (case 6)—Total blindness in the left eye and temporal hemianopia in the right eye, with bilateral primary atrophy of the optic nerve. There was probably a chiasmal lesion, the chiasm being split anteroposteriorly and the left optic nerve evulsed. In the right eye uncorrected vision was 20/70.

*Resume of Complaints and Findings*—The patient was forgetful, he exhibited changes in character, such as stubbornness and refusal to eat, there was blindness in the left eye, and disturbance of vision was noted in the right eye. No headache or dizziness was present. There were complete anosmia and advanced bilateral primary atrophy of the optic nerve, the disks were sharply outlined and chalky white, the veins were of moderate size, and the arteries were small. The left pupil did not react to direct light, the right reacted quickly to light. Determination of the visual fields on Oct 15, 1929, revealed blindness in the left eye and fairly complete temporal hemianopia in the right eye (fig 14). A suggestion of a Babinski sign and sporadic ankle clonus were present on both sides. The depressed fracture of the skull included almost the entire forehead. There was also a fracture into both orbits, apparently injuring the optic nerves. The blood pressure was 120 systolic and 70 diastolic.

A note written on Jan 28, 1929, by Dr Lloyd Mills, ophthalmologist, stated "The condition of this man's right optic nerve is such as to give much hope that

blurring of vision on the right side. The right pupil reacted well to light and in accommodation. The right fundus showed the margins of the disk to be clearly outlined, the veins rather full and the arteries small, there were no hemorrhages or exudates and no elevation. There was slight pallor of the disk. Rough testing showed no contraction of the visual field, but one gained the impression that the patient had a central scotoma. There was complete anosmia. Soon after the accident visual acuity in the right eye was 20/20, on July 24 it was 20/50.

On October 4 the patient still complained of pain in the right eye. He stated that objects looked as though he were seeing around a dark spot. He complained of occasional headaches, slight dizziness and no return of the sense of smell. The right pupil reacted well to light and in accommodation. The disk was somewhat paler than normal, anosmia persisted. The visual fields (fig 9) showed a scotoma of the right eye interfering with central vision. Vision in the right eye was 20/100. The blood pressure was 120 systolic and 76 diastolic.

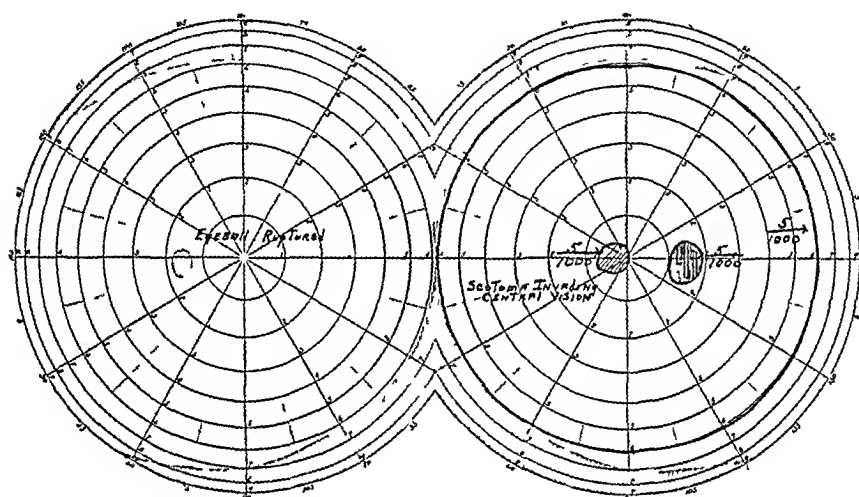


Fig 9 (case 1)—Paracentral scotoma on the right side, presumably due to damage to the macula, uncorrected vision in the right eye was 20/100+. The left eyeball was ruptured.

Röntgenograms of the skull showed a compound comminuted depressed fracture of the anterior wall of the frontal sinus, a linear fracture through the posterior wall of the sinus and a fracture across the bridge of the nose.

*Impression*—The following conditions were considered to be present: compound comminuted depressed fracture of the skull involving the frontal sinus and the bridge of the nose, rupture of the left eyeball, complete persistent anosmia, paracentral scotoma in the right visual field and slight pallor of the right disk.

*CASE 2*—Immediate monocular blindness following fracture of the left sphenoid wing and optic foramen. Subsequent recovery of an island of vision in the left lower nasal quadrant, primary atrophy of the optic nerve. Right visual field unaffected.

A. W. B., a man aged 30, single, an attorney, was referred by Dr. Leo M. Davidoff, of New York, on Oct. 6, 1933. The injury occurred on June 18, 1933, when the patient was thrown from a horse. He had no recollection of the accident and was unconscious for about nine days.



apparently developed after the injury and was still present fourteen months later. The Wassermann reaction of the blood was negative. Roentgenograms of the skull showed no evidence of fracture. Drs. Beigelman, Preston and Bullis expressed the following opinion: "The lesion in reference to the pupillary disturbance must be on the intercolated fibers between the anterior corpora quadrigemina and the Edinger-Westphal nucleus on the left side. The defect in the field is probably due to a lesion of the optic nerve anterior to the chiasm on the left side."

*Impression*—Injury to the left optic nerve anterior to the chiasm was considered to be present.

CASE 8—Complete blindness immediately following head injury. Subsequent bilateral primary atrophy of the optic nerve.

• W E P a man aged 49, married, a construction foreman, was referred by Dr. Roland Cummings on Jan 14, 1932. The patient was injured on July 6,

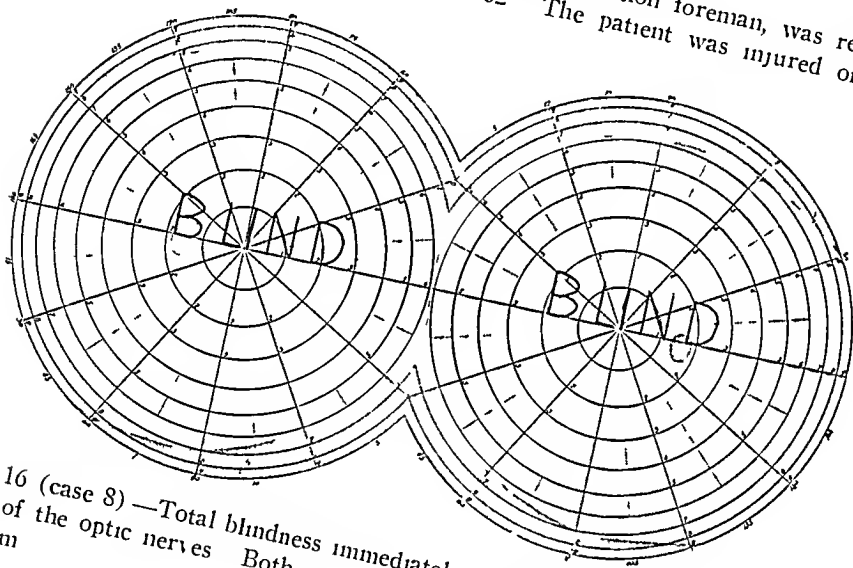


Fig 16 (case 8)—Total blindness immediately following head injury. Primary atrophy of the optic nerves. Both optic nerves were probably severed anterior to the chiasm.

1931, when he slipped and fell under a flat car of a narrow gage railroad and was dragged about 60 feet (18 meters). He was unconscious for about two and a half hours, and when he regained consciousness he was entirely blind. He sustained bruises across the bridge of the nose and "scraped off his right ear." His eyesight was said to have been good before the injury.

*Resumé of Complaints and Findings*—There was total blindness. The patient did not have the headache and dizziness so commonly present after a head injury. Examination of the fundi showed that both disks were sharply outlined and chalky white, the optic cups contained some new tissue, the veins were of good size, but the arteries were practically threadlike, the picture was typical of bilateral atrophy of the optic nerve (fig 16). The pupils were wide, round, regular, equal and fixed to light, they reacted little if any, in accommodation. The blood pressure was 140 systolic and 100 diastolic. Stereoscopic roentgenograms of the skull taken in the right lateral position showed considerable cloudiness in the region of the sella turcica, the posterior

1934, the visual field of the right eye showed no constriction, but there was marked loss of vision on the left side—there remained only an island of vision in the upper nasal portion of the field and there was loss of central vision (fig 11) Repeated subsequent examinations showed relatively little change in the visual fields Later there developed increasing pallor of both disks, this was especially marked on the left side At the time of writing the left disk is sharply outlined, almost chalky white, and shows an appearance typical of advanced primary atrophy of the optic nerve

Roentgenograms of the skull showed no fracture

*Impression*—The following conditions were considered to be present concussion, peripheral facial palsy on the right side and injury to the left optic nerve near the chiasm

*CASE 4—Blindness in the left eye immediately after head injury Subsequent primary atrophy of the optic nerve on the left side*

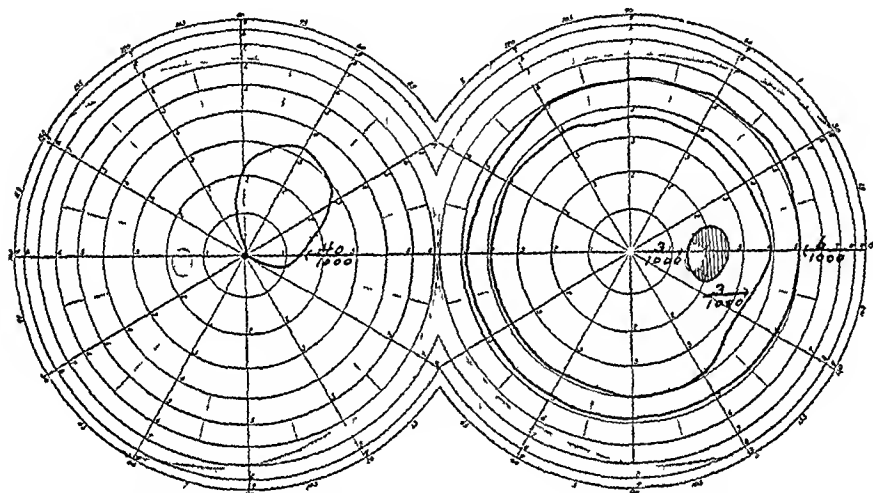


Fig 11 (case 3) —Remaining island of vision in the upper nasal quadrant of the left field, with lowered visual acuity, after a head injury The left optic nerve was presumably injured anterior to the chiasm With the left eye the patient saw a person as something shadowy at 15 feet (4.5 meters), in the right eye uncorrected vision was 20/40

H J F, a man, aged 35, married, a serviceman, was referred by Dr B C Adams, of Riverside, Calif., on Nov 5, 1933 The patient was injured on Sept 29, 1933, when his car went down a bank He recovered consciousness within a few minutes

*Resume of Complaints and Findings*—There were deafness in the right ear blindness in the left eye, numbness of the left side of the face, headache and dizziness partial anosmia in the right nostril, complete paralysis of the abducens nerve bilaterally, partial paralysis of the left trochlear and oculomotor nerves and of the right facial nerve, and motor and sensory disturbances referable to the left trigeminal nerve

Examination of the fundus of the right eye showed that the disk was sharply outlined and rather pale, the veins were within normal limits and the arteries were small, there were no hemorrhages, exudates or elevation In the left eye the

*Impression*—The following conditions were considered to be present: concussion of the brain, fracture of the right frontal region of the skull, diabetes insipidus, of traumatic origin, a chiasmal lesion, of traumatic origin, primary atrophy of the optic nerve, and bitemporal hemianopia.

*CASE 10*—*Right nasal hemianopia accompanying arteriovenous aneurysm of the right internal carotid artery and cavernous sinus, appearing approximately three months after injury*

A. H. L., a woman aged 46, married, a teacher, was referred by Dr. J. M. Nielsen on March 2, 1934. She was injured on Oct. 2, 1933, when she was struck by an automobile. She remembered being struck and thrown through the air, but she did not remember striking the pavement. She regained consciousness shortly afterward. She sustained a laceration of the scalp.

*Resume of Complaints and Findings*—The patient complained of generalized increasing headache, she was never free from discomfort in the head, she had attacks of sharp pain behind the right eyeball and stated that there was a feeling as though the eye would pop out, there was no observable bulging of the eye. The pain behind the eye was more severe when the patient was lying down, she slept propped up. Three months after the accident she noticed difficulty in vision consisting of blurring in the right eye, this increased when she lay down. There was no disturbance of vision in the left eye. At times the patient bumped into things on her left side. There was no ringing in the right ear except noises in the head.

Both fundi were within normal limits, the veins were full and pulsated on each side, the margins of the disks were clear. The pupils were equal and reacted well to light and in accommodation. The right eyeball was slightly more prominent than the left. The right palpebral fissure was a little wider than the left, there was no pulsation of the eyeball. When the patient lay down she experienced marked constriction of the nasal portion of the right field, almost amounting to nasal hemianopia, the left visual field was roughly normal. With the patient in the recumbent position a tongue blade (numbered from 1 to 9 from left to right) was held before her right eye. She saw the numbers on the right half but did not see those on the left half. When sitting up she saw all the numbers with the right eye until one compressed both jugular veins. When this was done she could no longer see the numbers to the left, but those to the right continued to be visible. When the right jugular vein alone was compressed she slowly lost sight of the numbers on the left end of the stick. If compression was firm enough to cut out the right carotid artery as well as the right jugular vein, there was no loss of vision. Similar tests carried out on the left side showed no disturbance of vision. Figure 18 shows the condition of the visual fields before and during compression of the jugular veins. The blood pressure was 140 systolic and 90 diastolic.

Roentgenograms of the skull showed no evidence of fracture. Dr. Blaine reported: "In the oblique position note is made of a definite difference in the size and shape of the optic foramen, the right one presents normal features on roentgen examination, while the left one is much larger than normal, there appears to be a bony density at the upper posterior quadrant of the right foramen, the exact significance of which I do not know but which suggests an enostosis."

Jan. 9, 1935, Dr. Nielsen stated that about six weeks subsequent to our examination the patient suffered from hiccup. She lay on her face in bed and held her breath. This was followed by intense pain behind the right eye and a noise in

*CASE 5—Blindness in the left eye following a gunshot wound of the head*

J M, a Mexican man aged 38, married, a laborer, entered the Los Angeles County Hospital on Jan 13, 1919 and was again seen in January 1935. The patient had sustained a gunshot wound in the left temple.

*Resume of Complaints and Findings*—There were complete paralysis of the oculomotor nerve and complete blindness in the left eye. The blood pressure was 136 systolic and 88 diastolic. The Wassermann reaction of the blood was negative.

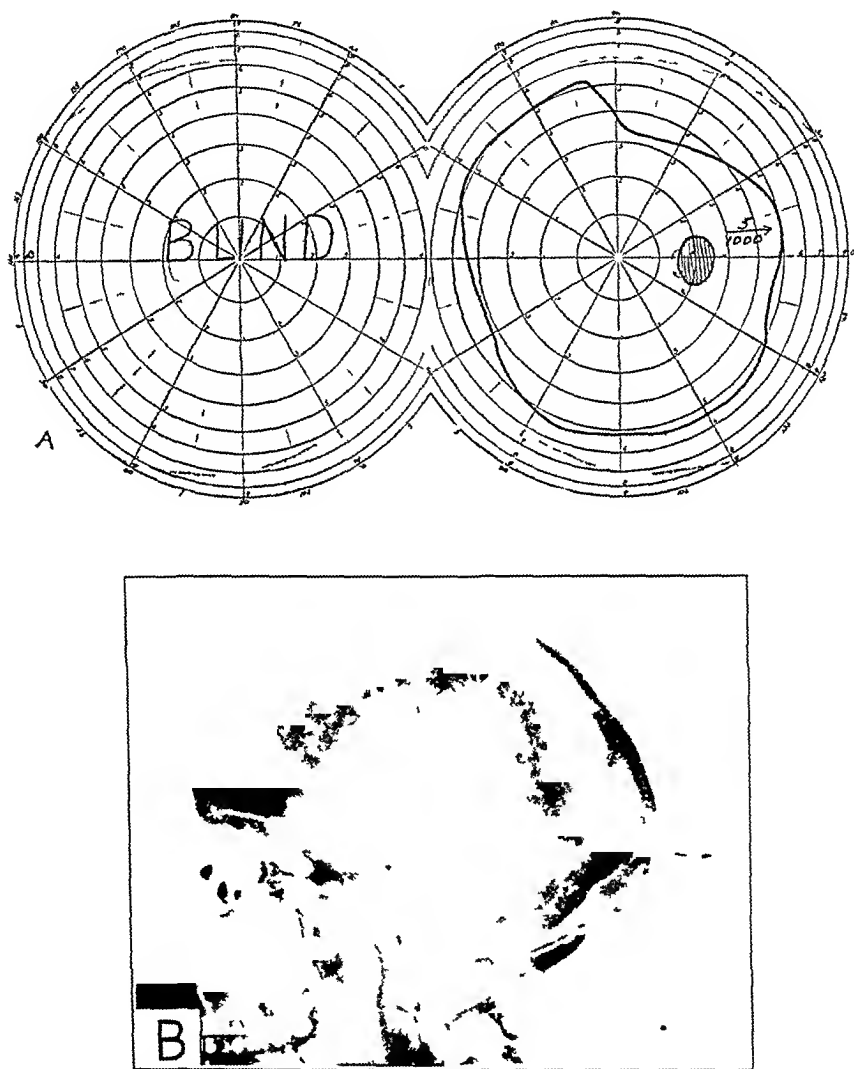


Fig 13 (case 5) — *A* immediate blindness in the left eye following a gunshot wound of the head. The left optic nerve was severed. *B* roentgenogram showing the position of the bullet near the chiasm.

Roentgenograms made in 1935 showed a metallic foreign body resembling a deformed bullet lying in the median wall of the left orbit in the region of the sphenoid sinuses. A trail of metallic fragments extended forward toward the base of the nasal bones. The main portion of the bullet lay immediately anterior to the sella turcica and somewhat toward the left. (The report on the roentgen examination was given by Dr R W Johnson.)

*Resume of Complaints and Findings*—The patient was unconscious for a short time immediately after the injury. On September 11 he became comatose and convulsions beginning in the right hand developed.

Examination disclosed weakness of the right hand. The pupils were unequal, the left pupil being larger than the right, both reacted to light. The eyegrounds showed overfilling of retinal veins, and the margins of the optic disks were somewhat obscured. The process was more marked in the left eye. On the right side there was hemiparesis, more marked in the upper extremity. The right knee jerk was more active than the left. There was a Babinski sign bilaterally. The spinal fluid was bloody.

Roentgenograms showed a long linear fracture crossing the left side of the skull from the occiput to the temple.

A large extradural clot was removed at operation on Sept 12, 1930.

The mother first noticed difficulty in the child's vision in September 1931, when he again started school. He seemed awkward and bumped into things.

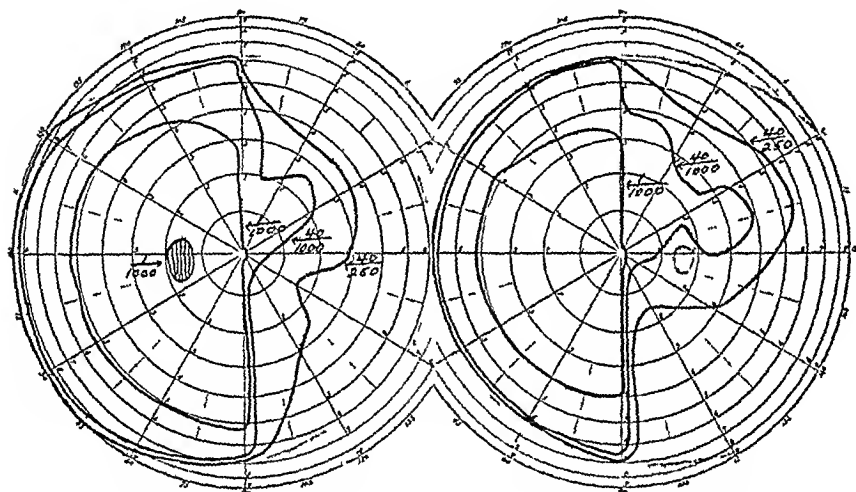


Fig 19 (case 11)—Right homonymous defects in the fields persisting more than four years after evacuation of a large extradural hematoma on the left side. Probable secondary subcortical lesion of the left temporal lobe. Corrected vision was 20/20—in the left and 20/15 in the right eye.

Glasses were fitted, but no improvement occurred. On Oct 1, 1934, Dr Clifford B. Walker, ophthalmologist, discovered a right homonymous defect in the fields (fig 19). I did not observe the defect while the child was under my care. This is not surprising, as the child was acutely ill at first and was too young to complain of moderate visual disturbance.

*Impression*—The following conditions were considered to be present: linear fracture of the skull and interval hemorrhage on the left side. It is probable that a second subcortical clot existed in the left temporal lobe.

*CASE 12*—Right lower homonymous defects in the fields following a blow on the head. Negative findings at operation.

J. C., a Mexican man aged 23, married, a laborer, was admitted to the Los Angeles County Hospital on Nov 1, 1934, after being struck with the butt of a revolver over the right temple.

there will be no further atrophic change. The color, while a little pale, is within normal limits, the nerve is well vascularized, and there is no particular change in the caliber of the retinal vessels. Visual function seems to be excellent within the limits of the fields which have been retained. In my opinion this will be retained permanently."

*Impression*—The following conditions were considered to be present: compound comminuted depressed fracture of the frontal region of the skull, concussion, contusion and laceration of the brain, fracture extending into both orbits, probably complete severance of the left optic nerve with resulting blindness, injury to the right optic nerve with resulting temporal hemianopia. It was believed that the injury to the optic nerves may have been near the chiasm.

*CASE 7—Temporal hemianopia of left eye persisting for fourteen months after injury*

J W, a man aged 34, married, a specialty distributor, entered the Los Angeles County Hospital on Oct 18, 1934. He was injured on Aug 31, 1933, when he was struck by a shovel above the left eye.

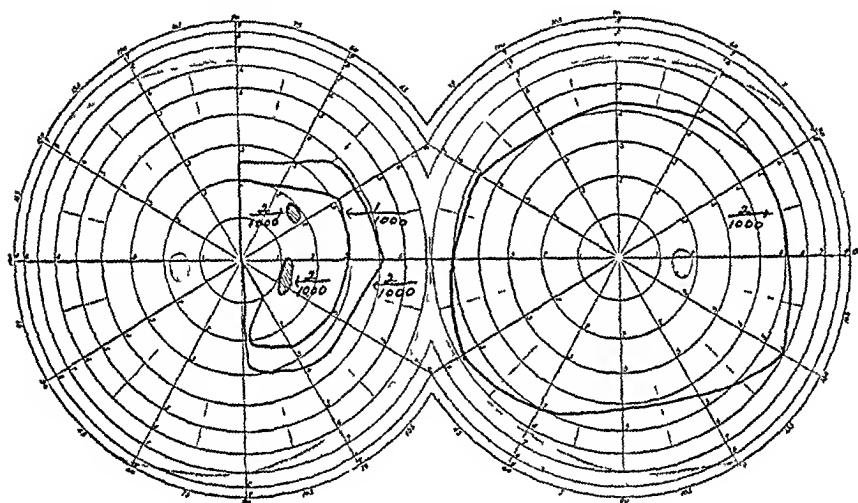


Fig 15 (case 7)—Temporal hemianopia in the left eye subsequent to head injury, probably caused by direct injury to the left optic nerve near the optic foramen. With the left eye the patient could not count fingers at 20 feet (6 meters), in the right eye corrected vision was 20/20.

*Resume of Complaints and Findings*—The patient was unconscious for an unknown length of time. After recovering consciousness he complained of headache, dizziness, inability to see with the left eye and pain in the right side of the face. This pain had the usual characteristics of a trigeminal neuralgia and was confined to the infra-orbital distribution. Several injections of alcohol failed to give relief in spite of the fact that characteristic numbness was obtained.

Except for the changes in the visual fields and the symptoms of involvement of the left trigeminal nerve the results of the neurologic examination were negative. The left pupil did not react to direct light but reacted consensually, the right pupil reacted to direct light but did not react consensually. The fundi were normal. There were no retinal detachments. The macular region, the nerve head and the vessels were normal. Vision in the right eye was 20/20, with the left eye the patient was unable to count fingers at 20 feet (6 meters). On Oct 21, 1933, the visual fields showed a temporal hemianopia on the left (fig 15), which

I P, a woman aged 20, divorced, a waitress, was admitted to the Los Angeles County Hospital on March 16, 1935. She was injured on March 5, 1935, when she fell backward, striking her head on the pavement.

*Resumé of Complaints and Findings*—The patient remained unconscious for about ten minutes. She suffered from headache for a day or more, this was followed by an interval of about four days when she felt quite herself. The headache returned in the left temporal region and increased daily in severity. On about March 12, 1935, the patient noticed drooping of the left eyelid and slight weakness of the left arm and leg. During the next three days headache increased and she became stuporous.

On admission she was stuporous. There was marked palsy of the left oculomotor nerve with ptosis, the pupil was dilated and fixed, and outward rotation of the eye was noted. Marked paresis and increased deep reflexes were present on the left side. There was a Babinski sign on the left, but not on the right, side.

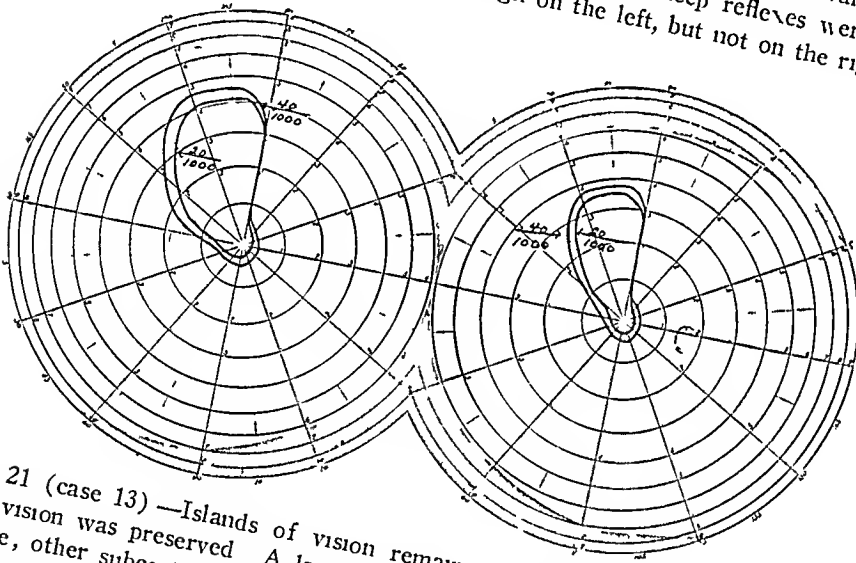


Fig 21 (case 13)—Islands of vision remaining in the upper left quadrants. Central vision was preserved. A large subdural hematoma was evacuated on the right side, other subcortical lesions were suspected. Uncorrected vision was 6/10 in both eyes.

The spinal fluid was under a pressure of 400 mm and was slightly bloody. The Wassermann reaction of the blood was negative. The blood pressure was 132 systolic and 86 diastolic.

Roentgenograms of the skull failed to reveal a fracture. On March 17, 1935, Dr R B Raney explored the left temporal region and found a large chronic subdural hematoma in process of formation. The contents were scooped out. A button opening was then made over the right temporal region, but no hematoma was encountered.

On March 27, 1935, study of the visual fields showed that vision remained only in the upper left quadrants (fig 21), in other words, there was complete right homonymous hemianopia and a lower left quadrantal defect. The eyegrounds showed marked blurring of the disks, with filling of the optic cups, distention of the vessels and elevation of about 2 diopters. Visual aphasia developed. A subsequent

clinoid processes were hazy No fracture of the skull was seen Stereoscopic roentgenograms taken in the anteroposterior position failed to show a fracture of either orbit

*Impression*—The following conditions were considered to be present concussion of the brain and immediate total blindness, probably due to severance of the optic nerves at the chiasm (This is the only case of total blindness in this series)

*CASE 9*—*Bitemporal hemianopia, probably due to splitting of the optic chiasm anteroposteriorly, following head injury Bilateral primary atrophy of the optic nerve of moderate degree*

A F, a man aged 34, married, a chef, was referred by Dr Joseph Jacobs on Dec 15, 1931 He was injured on Nov 17, 1931, in a collision of his automobile and a freight train He is said to have been unconscious for several days He bled from the left ear and had severe headache, nausea and vomiting the first few days

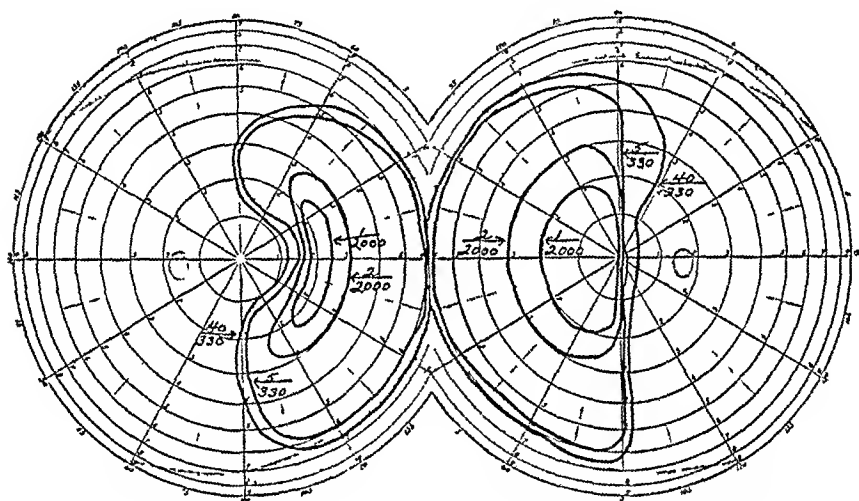


Fig 17 (case 9) —Bitemporal hemianopia subsequent to chiasmal lesion The chiasm was presumably split in an anteroposterior direction Corrected vision was 20/200 in the left and 20/30— in the right eye

*Resumé of Complaints and Findings*—The patient had delusions regarding relatives, lapses of memory, difficulty in seeing, especially with the left eye, and abnormal thirst

There were bitemporal hemianopia, diabetes insipidus, the patient drinking about 9 quarts (85 liters) of water a day and excreting an equal amount of urine, and mental confusion regarding the accident The eyegrounds showed definite pallor of both disks, the picture suggesting an early stage of primary atrophy of the optic nerve, more marked on the left than on the right The hemianopia was more complete on the left than on the right (fig 17) The pupils were wide and equal and reacted poorly to light and in accommodation The blood pressure was 140 systolic and 100 diastolic The fields subsequently improved with diathermy administered under Dr Clifford B Walker's direction

Roentgenograms of the skull showed a long linear fracture in the right frontal region with a slight depression



unequal, the left being somewhat larger than the right. The left pupil reacted sluggishly to light, the right one reacted actively. There was still complete paralysis of the left abducens nerve. The right fundus showed a sharply outlined, pale disk with new tissue in the optic cup. The veins were of average size, the arteries were small. The left fundus was less distinctly seen, because of haziness of the cornea and media. The disk, however, appeared to be pale, the arteries were small. The visual fields showed a typical left homonymous hemianopia with marked contraction of the nasal field on the left. Visual acuity on the left was greatly reduced (fig 22).

*Impression*—The following conditions were considered to be present: concussion and contusion of the brain, possible fracture of the midmaxillary region, paralysis of the left abducens nerve, bilateral secondary atrophy of the optic nerve, and left homonymous hemianopia. The lesion was presumed to be in the left optic tract just posterior to the chiasm.

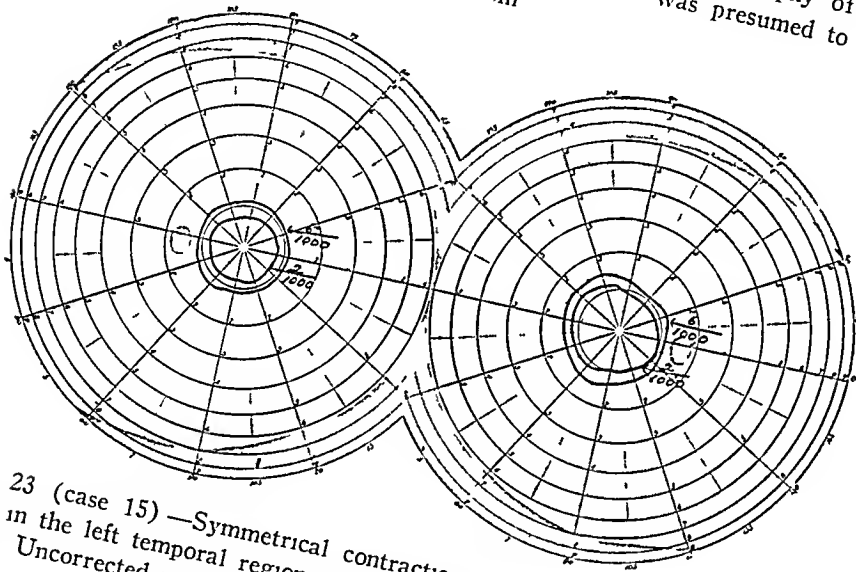


Fig 23 (case 15)—Symmetrical contraction of the fields two months after fracture in the left temporal region. Examination was made when litigation was pending. Uncorrected vision was 20/70 and corrected vision 20/30 in both eyes.

**CASE 15**—Symmetrical contraction of the fields appearing about two months after fracture of the skull.

A McH, a woman, aged 65, single, a practical nurse, was referred by Dr Cortland Myers on Aug 22, 1934. She was injured on August 1, when she fell down a flight of stairs. She sustained a fracture of the left wrist but was not rendered unconscious.

*Resume of Complaints and Findings*—There were dizziness, severe pain in the left side of the head, unsteadiness of gait, ringing in the left ear and photophobia.

There was tenderness in the left temporal and parietal regions. The pupils were equal and reacted well to light and in accommodation. On Aug 22, 1934, the visual fields showed no constriction on rough tests. By October 17 they showed marked concentric constriction, which was borne out by perimetric studies (fig 23). The patient also complained of photophobia. (A law suit was pending at this time.) The blood pressure was 195 systolic and 100 diastolic.

the head. The right eye became more prominent and remained so for a number of weeks. Subsequently the subjective murmurs in the head disappeared, the eyeball receded, and the aforementioned visual disturbances cleared up.

*Impression*—Posttraumatic arteriovenous aneurysm of the left internal carotid artery and the cavernous sinus was considered to be present.

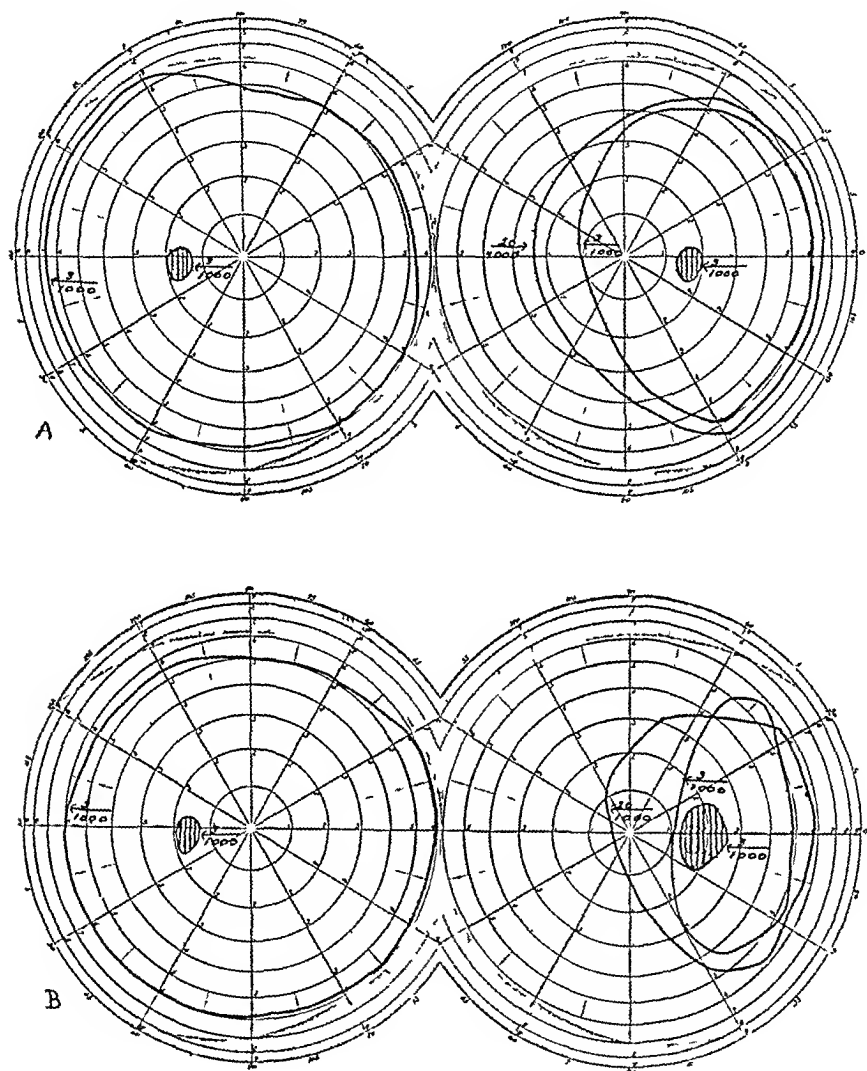


Fig 18 (case 10)—*A*, nasal contraction of the field of the right eye subsequent to traumatic arteriovenous aneurysm when no compression was applied to the jugular veins, *B*, marked increase of the visual defects following compression of the jugular veins. Vision was 20/20+ in both eyes.

*CASE 11*—*Right homonymous defects following extradural hemorrhage on the left side, subsequent improvement*

I C, a schoolboy aged 6, was referred by Dr Hugo M Kersten on Sept 12, 1930. He was injured on Sept 9, 1930 when he fell from a swing at school.

Roentgenograms of the skull showed a fracture on the left side, beginning near the midline of the superior portion of the occipital bone, extending laterally downward and forward, crossing the parieto-occipital suture and the superior portion of the left mastoid region and entering the region of the petrous portion of the temporal bone, where it faded out

*Impression*—The following conditions were considered to be present: concussion of the brain, fracture of the skull, complete anosmia (organic), deafness in the left ear (organic), and hysterical contraction of the left visual field. The case presented furnishes an example of functional, superimposed on organic, changes

CASE 17—*Hysterical contraction of the fields appearing eight months after fracture of the skull*  
W G, a man aged 26, single, a laborer, was referred by the Associated Indemnity Corporation on Sept 12, 1934. The patient was injured on March 24,

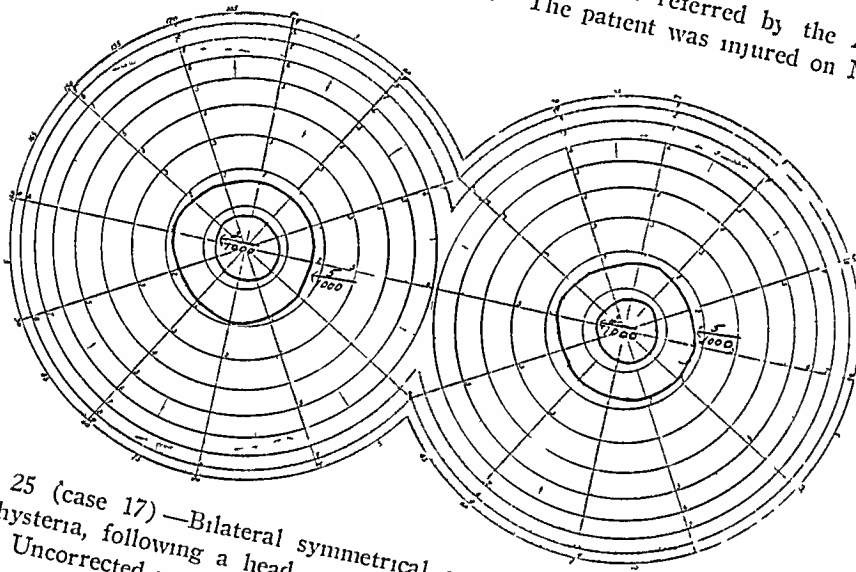


Fig 25 (case 17)—Bilateral symmetrical contraction of the fields, probably due to hysteria, following a head injury. Many other neurotic symptoms were present. Uncorrected vision was 20/50 in both eyes.

1934, when he was thrown 10 feet (3 meters) from a tram bucket and struck his head on some rocks. He was unconscious for about six hours. Both eyes were swollen shut, and both wrists were fractured.

*Resume of Complaints and Findings*—On September 12 the patient complained of headaches, dizziness, anosmia and disturbance in taste. Examination revealed complete anosmia. The pupils were equal and reacted well to light and in accommodation. The eyegrounds were normal. On November 21 the patient first complained of blurred vision, he could read only headlines of the newspaper. The visual fields showed symmetrically concentric contraction of a hysterical type (fig 25). The patient was beginning to show signs of neurosis. On December 21 he still had contracted fields, but to a less marked degree. The blood pressure was 125 systolic and 60 diastolic. Roentgenograms of the skull showed a fracture crossing both frontal sinuses, with a second line extending to the bridge of the nose and crossing the right orbit.

*Resume of Complaints and Findings*—On admission the patient was stuporous. The right pupil was dilated and static, the left was mobile. There was moderate spasticity on the left side, all the deep reflexes on the left being more marked than those on the right. The spinal fluid was bloody and was under increased pressure. The Wassermann reaction of the blood and that of the spinal fluid were negative. The patient improved quite rapidly and was discharged on Dec 12, 1934. He returned on Dec 16, 1934, complaining of inability to see with the left eye, of continuous headache in the frontal region, of dizziness and of general weakness.

Roentgenograms showed no fracture of the skull.

On Dec 20, 1934, it was again noted that the right pupil was larger than the left, both reacted well to light. The deep reflexes on the right were increased as compared with those on the left (just the opposite of what was present on the first admission). There were a Babinski sign and a Chaddock sign on both sides.

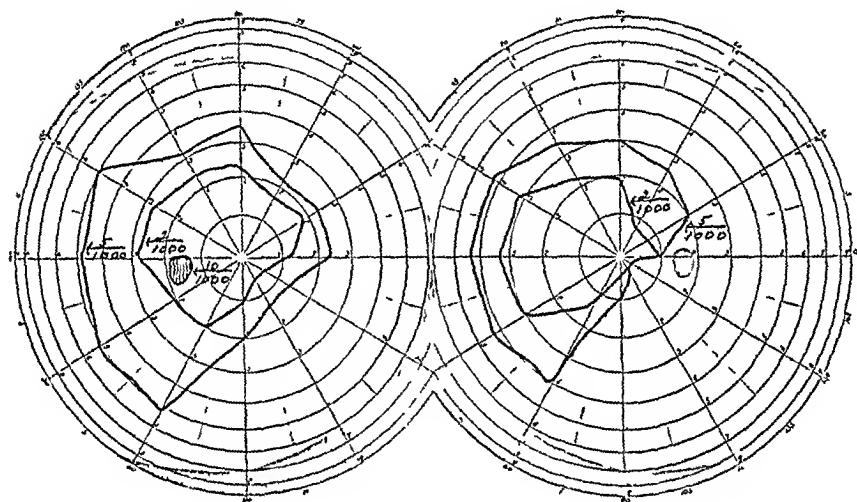


Fig 20 (case 12)—Right lower homonymous defects in the fields subsequent to head injury. No subdural hemorrhage was encountered at operation, the defect was believed to be due to subcortical hemorrhage in the left occipital lobe. Subsequent improvement occurred. Corrected vision was 20/20 in the left and 20/70 in the right eye.

On Jan 12, 1935, the patient had generalized convulsions, and at times he had difficulty of speech. The pulse rate dropped as low as 40. On Dec 8, 1934, the spinal fluid was clear and colorless, the pressure was 120 mm, the cell count 2 and the Nonne test negative.

A perimetric study made on Jan 15, 1935, showed a suspicious right homonymous contraction of the visual fields. A second study, made on Jan 22, 1935, showed an increase of the right homonymous defect in the fields (fig 20). During the next two weeks vision improved. On Jan 23, 1935, multiple trephine openings were made on each side of the skull, no hematoma was discovered.

*Impression*—Probably there was a chronic subdural hematoma on the left side.

CASE 13—Islands of vision remaining only in the upper left quadrants after head injury.

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CASE 19—Probable hysterical contraction of the field following concussion of the brain

E C, a Negro aged 32, married, a laborer, was referred by Dr J Rollin French on Dec 15, 1931. He was injured on about Oct 15, 1930, when he was struck on the top of the head by a falling iron roller. He had no recollection of the accident, retrograde amnesia was present for several hours. He was unconscious for about six hours and hospitalized for twenty days. He attempted to work two months after being injured, but stopped after one week because of severe headache.

*Resume of Complaints and Findings*—There were headaches, pain behind the eyes, burning of the eyes, blurring vision and photophobia. The pupils were round, regular and equal and reacted sluggishly to light but well in accommodation. There was marked photophobia. The eyegrounds showed overfilling of the veins, the arteries were full, the margins of the disks were

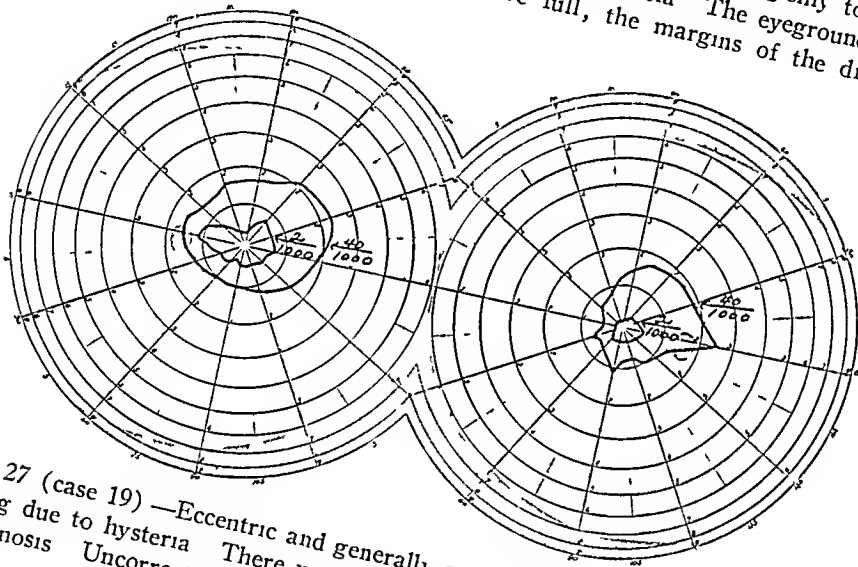


Fig 27 (case 19)—Eccentric and generally contracted fields, the defects probably being due to hysteria. There were many other neurotic symptoms to support this diagnosis. Uncorrected vision was 20/50 in both eyes.

slightly hazy. There were no hemorrhages or exudates and no elevation. Marked contraction of both visual fields was seen by rough testing. Perimetric charting on Jan 15, 1931, revealed marked but somewhat irregular, not typically tubular, contraction of the fields (fig 27). Acuity of vision was diminished, being 20/50 in the left and 20/50 in the right eye. The Wassermann reaction of the blood was negative. The blood pressure was 140 systolic and 90 diastolic. Roentgenograms of the skull showed no fracture.

*Impression*—Concussion of the brain, photophobia and hysterical contraction of the visual fields were considered to be present.

CASE 20—Superior homonymous hemianopia probably of functional origin, following head injury. Great fluctuation in type of fields over a period of five years. H H, a man aged 41, married, a laborer, was referred by the Maryland Casualty Company on April 8, 1930. He was injured on Sept 21, 1929, when he fell from the top of a box car, striking his head. He was unconscious for about two weeks and was hospitalized for eight weeks.

trepine opening over each occipital lobe failed to reveal a hemorrhage. Ventriculography showed normal-sized ventricles, which were not displaced.

*Impression*—The supposition that bilateral chronic subdural hematoma was present was not borne out on exploration. Bilateral subcortical hemorrhage in the temporal or occipital lobe may have caused the picture. The probability that a chiasmal lesion existed seemed remote.

*CASE 14—Left homonymous hemianopia more than six months after head injury. Paralysis of the left abducens nerve. Advanced secondary atrophy of the optic nerve.*

M. B., a widow aged 36, a housewife was referred by Dr. Frank D. Sweet of Long Beach, Calif., on Oct. 31, 1934. She was injured on Oct. 15, 1934 in an automobile collision. She remained comatose or semicomatose for a number of weeks, hospitalization being necessary for more than two months.

*Resume of Complaints and Findings*—The patient was disoriented as to time and place for several days. When the mental symptoms cleared she complained of headache and double vision. Later she complained of half vision in the left eye.

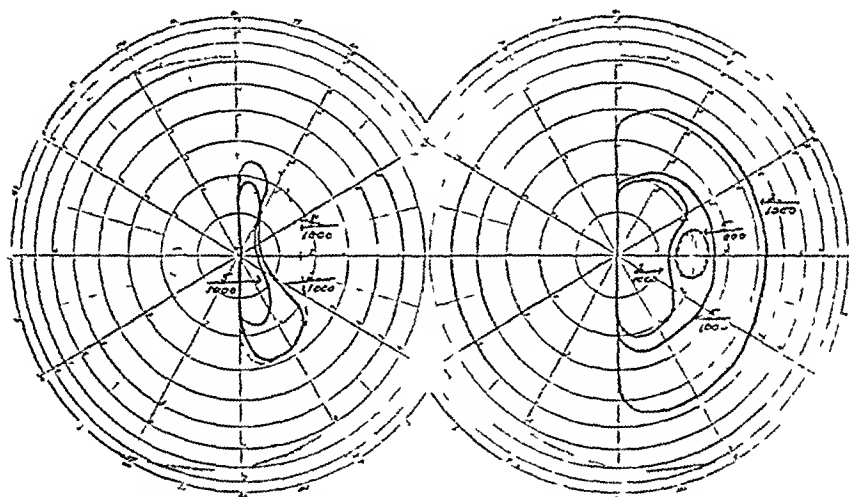


Fig. 22 (case 14)—Left homonymous hemianopia present six months after head injury. There was bilateral atrophy of the optic nerve, probably secondary. The lesion was believed to have affected the right optic tract just behind the chiasm. With the left eye the patient saw the card as something light at 20 feet (6 meters). In the right eye uncorrected vision was 20/30.

At the time of the first examination complete palsy of the left oculomotor nerve existed. The left pupil was much larger than the right one and reacted little to direct light but well consensually. There was complete ptosis of the upper lid. The left eye could not be turned outward beyond the midline as there was complete paralysis of the abducens nerve. Vision in the left eye was low. The details of the left fundus were indistinct, but the disk seemed a little pale. The right fundus showed a clearly outlined disk with arteries and veins within normal limits. The blood pressure was 110 systolic and 40 diastolic.

Roentgenograms of the skull failed to reveal a fracture of the vault. A suspicious line running anteroposteriorly between the maxillary antrums was noted. This may have represented a fracture.

The patient was reexamined on April 10, 1935. At that time the palsy of the oculomotor nerve had practically cleared up. The pupils however were still

jerks were greater on the left than on the right side. Other superficial and deep reflexes were normal. No contraction of the visual fields was revealed by rough tests in September 1929. The blood pressure was 120 systolic and 80 diastolic. The Wassermann reaction of the blood was negative. Roentgenograms showed an extensive T-shaped fracture in the right frontal region.

On Oct 5, 1931, the patient was found throwing his head back and squinting, at other times he stared, he cooperated poorly. Rough tests showed constriction of the visual fields. Perimetry showed a superior hemianopia of each eye, the patient being unable to see above the midline except at the fixation point, where he saw about 3 degrees above the center. Vision was 20/50 in the left and 20/50 in the right eye. Moderate pallor of the disks was noted. On May 22, 1933, impairment of the upper fields in both eyes was again present, on that date vision was 20/70 in the left and 20/50 in the right eye (fig 28). On April 26, 1934, the patient still complained of headache, dizziness, deafness and difficulty in seeing. There was anosmia in the left nostril but not in the right. This was a new finding. The disks were possibly paler than before. The visual fields showed not only hemianopia of the upper half of each field but also marked contraction of the lower fields, which was not present before.

*Impression*—The following conditions were considered to be present: concussion and contusion of the brain, extensive fracture of the right frontal region of the skull, impairment of hearing, especially on the right side, definite changes in character and memory, and superior homonymous hemianopia, probably functional.

*CASE 21*—*Central scotoma and contraction of the right visual field observed immediately after head injury. Slight macular edema and advanced arteriosclerosis of the right fundus. Subsequent inferior hemianopia of the right eye and development of manifestations of hysteria.*

W H L, a man aged 60, married a salesman, was referred by the Liberty Mutual Insurance Company on Oct 29, 1934. The injury occurred on May 9, 1934, when the patient's automobile went off an embankment. He remained in a semistuporous condition for approximately two weeks.

*Resume of Complaints and Findings*—The patient complained of headache, dizziness, impairment of memory, unsteadiness in walking and difficulty in seeing with the right eye. On June 12, 1934, Dr John C Williams, of San Francisco, described a scotoma in the right eye. On Aug 28, 1934, Dr Otto Barkan, of San Francisco, described arteriosclerotic changes of the retina and a small central scotoma in the right eye. A few patches of scotoma in the midperipheral region were described. The left field was said to be normal (fig 29). Suddenly, on the evening of Sept 12, 1934 (four months after the accident), the patient lost the use of his right arm and leg, and right hemianesthesia developed. He was again able to walk at the end of a month but needed help.

There was anosmia in the right nostril. The pupils were equal and reacted well to light and in accommodation. The eyegrounds showed moderate arteriosclerotic changes but were otherwise normal. Determination of the visual fields on Oct 29, 1934, revealed a bizarre type of hemianopia. There was complete right hemianesthesia (fig 30). The patient used the right hand and leg awkwardly. The gait was peculiar in that he threw his right leg in front of him. In spite of awkwardness during voluntary use, involuntary gestures were made normally with the right hand. The abdominal and epigastric reflexes were not obtained. All the

Roentgenograms of the skull showed a fine linear fracture in the left temporal region

*Impression*—The following conditions were considered to be present linear fracture in the left temporal region, subsequent functional disturbance of the visual fields, probably suggested by pending litigation

CASE 16—*Tubular vision in the left eye following fracture of the skull Other neurotic manifestations*

O W, a man aged 26, married, an oiler, was referred by Dr R O Schofield, of Boulder City, Nev, on April 26, 1933 The patient was injured on May 7, 1932, when he was thrown out of a truck and rendered unconscious He recovered consciousness seven days later There was bleeding from the left ear He remained in the hospital six weeks, returning to work in a tool room in August 1932 By April 1933 he was working on a power saw

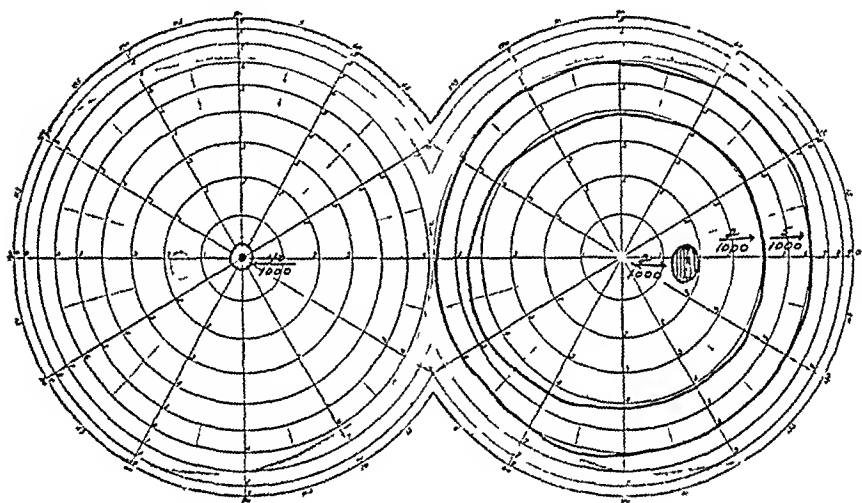


Fig 24 (case 16)—Tubular vision in the left eye (the central dot represents a large fixing object and not a scotoma) eleven months after a fracture of the skull With the left eye the patient saw the card as something blurred at 20 feet (6 meters), in the right eye uncorrected vision was 20/30+ This patient had many other neurotic manifestations

*Resume of Complaints and Findings*—There were pain in the back of the neck, stiffness of the neck, headache, dizziness, deafness and ringing in the left ear and blurred vision in the left eye

There was complete bilateral anosmia The right fundus was normal, the left could not be examined as the patient closed the eye The pupils were unequal, the left pupil being larger than the right, both reacted to light, but the right reacted more quickly than the left Consensual action was good in both eyes The ticking of a watch was not heard when the watch was pressed against the left ear, it was heard at 2 inches (5 cm) from the right ear A tuning fork was not heard by air conduction or bone conduction on the left, air conduction was better than bone conduction on the right Weber's test showed the sound referred to the right The blood pressure was 130 systolic and 80 diastolic Determination of the visual fields on April 26, 1933, showed marked hysterical contraction on the left (fig 24)



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onset of right hemianesthesia four months after injury was believed to be functional. The early changes in the field were scotomas on the right side, the later changes consisted of a bizarre inferior hemianopia. The latter was construed as a functional condition.

CASD 22—*Moderate concentric contraction of the left visual field with other manifestations of hysteria occurring nine months after injury and coincidental with return to heavy work.*

J S R, a man aged 26, married, a rotary helper, was referred by the State Compensation Insurance Fund on April 19, 1934. He was injured on Feb 11, 1934, when a derrick collapsed and he was thrown into the ocean. He sustained

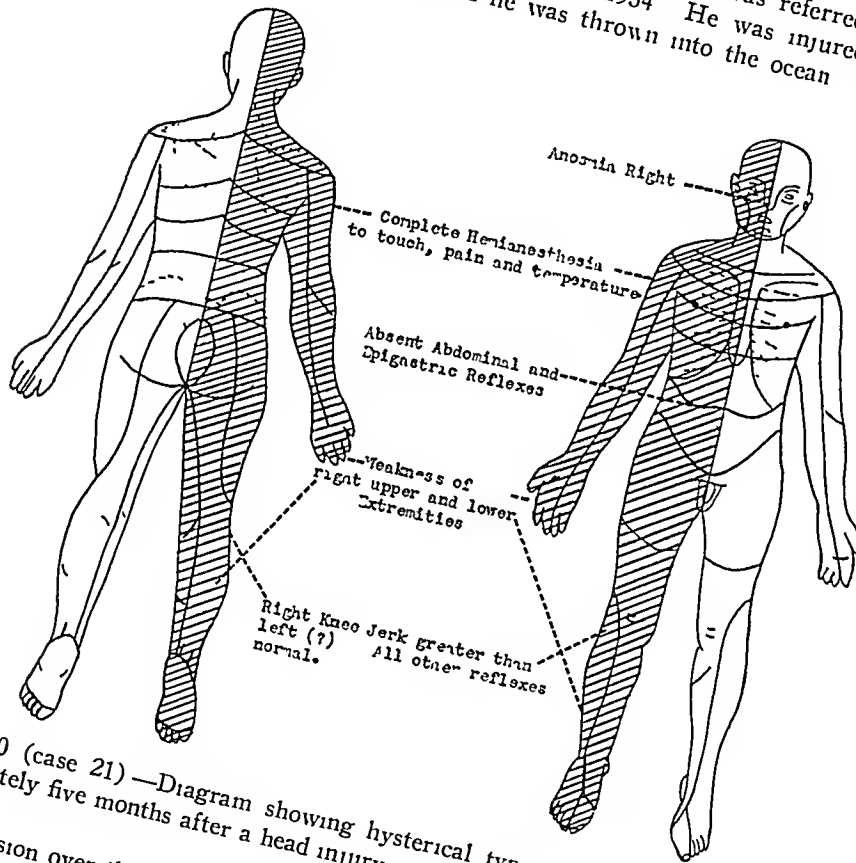


Fig 30 (case 21)—Diagram showing hysteric type of anesthesia appearing approximately five months after a head injury

a deep abrasion over the left eyebrow and left eyelid and was unconscious for about three hours

*Resumé of Complaints and Findings*—There were headaches in the left frontal region and marked dizziness on stooping or on sudden change of position. There was a scar in the left eyebrow showing the imprint of pipe threads. The pupils reacted well to light and in accommodation. The fundi were normal. The blood pressure was 130 systolic and 70 diastolic. The patient returned to work, roughnecking, on Oct 20, 1934, and continued working until November 6. This was heavier labor than should have been given him. Headaches and dizziness were immediately increased. There developed hypesthesia of the entire left side, including relative anosmia in the left nostril.

*Impression*—Fracture of the skull and concussion of the brain were considered to be present. Changes in the field due to hysteria appeared eight months after injury.

CASE 18—*Tubular vision appearing six weeks after head injury*

O. E. T., a man aged 39, married, a motorcycle officer, was referred by the State Compensation Insurance Fund on Oct 9, 1934. The patient was injured on Aug 2, 1934, when he was thrown from his motorcycle. He did not recover full consciousness for fifteen days.

*Resume of Complaints and Findings*—On Oct 9, 1934, the patient complained of marked dizziness and headache.

Examination revealed complete anosmia. The fundi showed overfilling of the veins and new tissue in the optic cups. The pupils were equal and reacted well to light and in accommodation, extra-ocular movements were normal. Ticking of a watch was heard 2 inches (5 cm.) from the right ear, it was not heard when

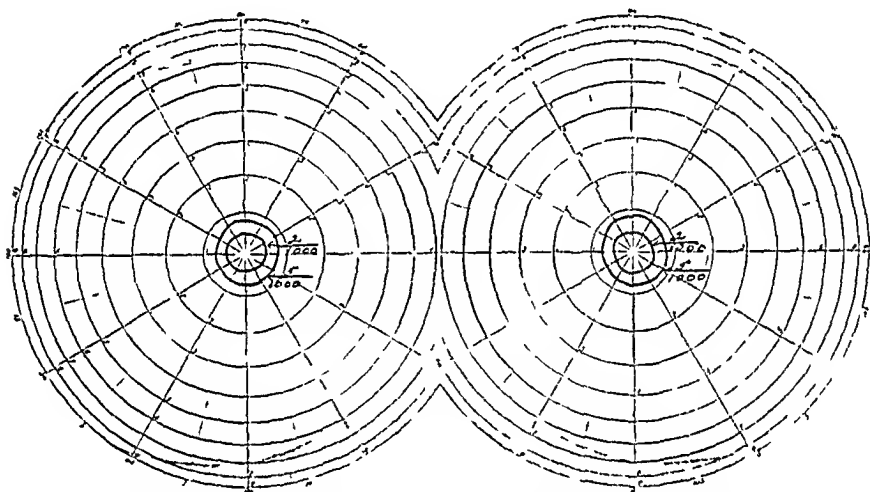


Fig 26 (case 18)—Tubular vision present three months after a severe head injury. The patient was slightly neurotic. Uncorrected vision was 20/30 in the left and 20/20++ in the right eye.

the watch was pressed against the left ear. There was no history of bleeding from the ears. Tests with tuning forks showed that air conduction was better than bone conduction on both sides. The Weber test showed that the sound was not referred. The Romberg sign was strongly positive. All the deep reflexes were active and equal, and there were no abnormal reflexes. There was no constriction of the visual fields on rough tests. The blood pressure was 120 systolic and 80 diastolic.

On November 20 the general condition was improved, but the patient complained of watering of the eyes. Rough testing of the visual fields showed concentric contraction, which was brought out by perimetric studies (fig 26). The fields improved when the patient returned to light work, four months later.

Röntgenograms of the skull revealed no fracture.

*Impression*—The following conditions were considered to be present: concussion and contusion of the brain, anosmia, superimposed neurosis with hysterical contraction of the visual fields.

## ARCHIVES OF SURGERY

bumped his head against an iron flange. He was said to have been unconscious for twenty minutes. In spite of severe headache he returned to work the following day. After working for two days he was obliged to stop. A period of headache and dizziness followed. Three days after the injury there developed blurring of vision in the right eye, as well as diplopia, which lasted ten days.

*Resume of Complaints and Findings*—There were headaches, dizziness and blurring of vision in the right eye. The fundi showed fulness of the veins, some new tissue in the optic cups and sharp disk margins. The pupils reacted well to light and in accommodation. There was constriction of the right temporal field as judged by rough tests. The abdominal and epigastric reflexes were quicker on the right than on the left. The blood pressure was 130 systolic and 80 diastolic. The Wassermann reaction of the blood was negative. The visual fields showed general constriction.

Roentgenograms of the skull showed no evidence of a fracture. On April 29, 1933, there was severe headache. The right eye again "went blind" for a minute or two. The patient returned on May 16, 1933. He had been doing light work since January 1932. The pupils were equal and reacted quickly to light and in accommodation. The eyegrounds were normal. The abdominal and epigastric reflexes were equal. There was moderate hypesthesia to touch, pain and temperature over the entire left side of the body (fig 32). This was a new finding. The right visual field still showed marked contraction, but there was definite improvement in the left (fig 32).

*Impression*—Moderate concussion of brain and residual manifestations of hysteria were considered to be present.

CASE 24—*Hysterical contraction of the left visual field following fractures extending into the left orbit. Improvement nine years later.*

A S., a man aged 51, married, a stunt actor, was referred by Dr. John D. Gillis on Nov 3, 1923. The patient had been kicked in the head by a horse, being immediately rendered unconscious. There was bleeding from the nose but not from the ears.

*Resume of Complaints and findings*—There was a 2 inch (5 cm) laceration in the left frontal region. After sustaining the injury the patient remained in a semicomatose condition for three or four days. A decompression was performed on November 7 and revealed a tight, wet brain. The patient remained irrational for about three weeks. His convalescence was unsatisfactory and slow. The Wassermann reaction of the blood was negative.

Roentgenograms showed an extensive stellate fracture in the left frontal region which ran down into the temporal bone and "behind the left orbit." This patient was followed for about five years. During that time he presented many mental aberrations, changes in memory, disturbances of orientation and periods of euphoria. He insisted that he was blind in the left eye from the time that he recovered consciousness. The eyegrounds appeared essentially normal on early examination, but as time went on the left disk showed increasing pallor. Moderate advancing primary atrophy of the disk was considered to be present. Dr. Lloyd Mills, ophthalmologist, also observed the patient and in a report on an examination made on Dec 22, 1923, described the right fundus as essentially normal. On the left he found moderate atrophy of the choroid near the terminal twigs of certain retinal vessels. He also found moderate whitening of the left optic nerve, with temporal absorption of its head. Moderate arteriosclerotic changes were evident. The central changes in the choroid were considered non-

*Resume of Complaints and Findings*—There were changes in disposition, forgetfulness, impairment of hearing, headaches, dizziness and double vision

The fundi were normal save for slight pallor of the disks. The pupils were equal and reacted well to light and in accommodation. There was diplopia on looking to the right, to the left and upward. There was bilateral deafness, greater on the right than on the left side. Tests with tuning forks showed that bone

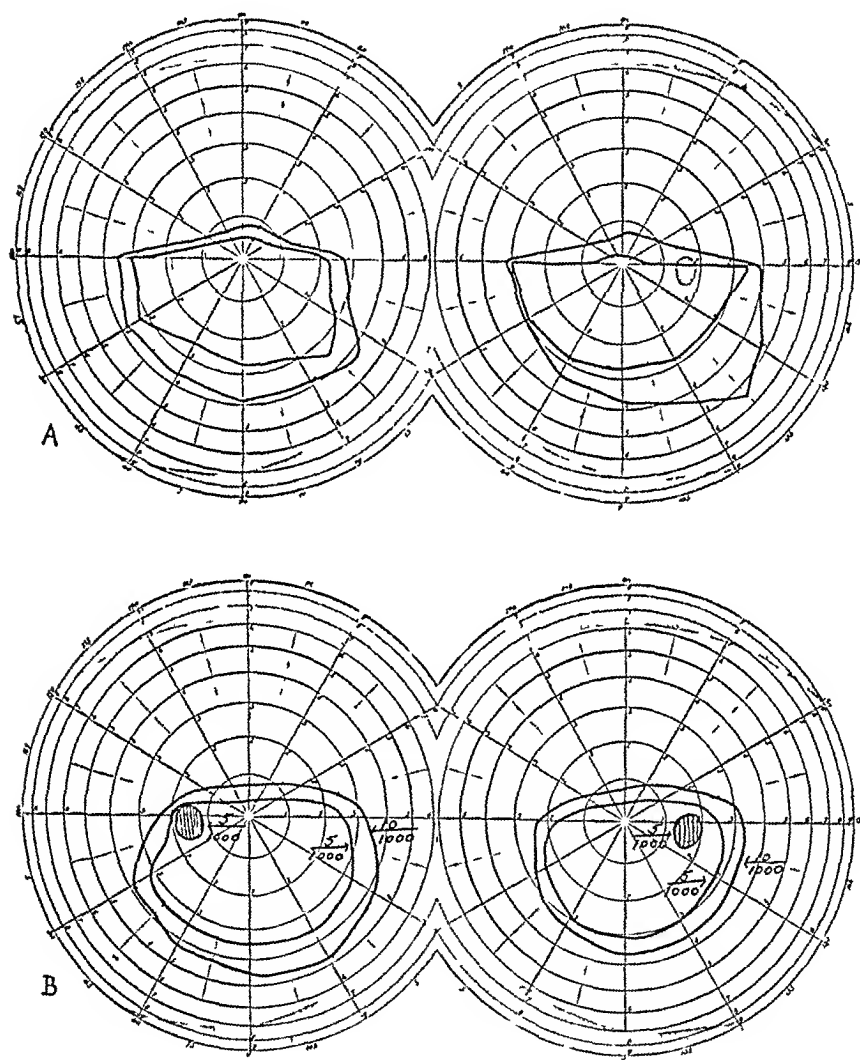


Fig 28 (case 20)—Visual fields taken by different observers. *A*, fields in 1931, *B*, fields in 1935. In spite of the upper hemianopic defects the picture presented by the fields is believed to be due to hysteria. The development of many other neurotic symptoms supports this view. The representation of the right field in *A* was transferred from the universal perimeter. At the second examination (*B*) uncorrected vision was 20/40 in the left and 20/30 in the right eye.

conduction was better than air conduction on the right but that air conduction was better than bone conduction on the left side. The Weber test showed the sound referred to the right. The mental reactions were slow. The biceps and triceps

(fig 32), at other times the patient stated that he did not feel pin prick over any extremity or, in fact, over the body, on still other occasions the sensory picture appeared normal. No discrepancies of note were ever found in the reflexes. The mentality remained childish throughout the period of observation.

*Impression*—The following conditions were considered to be present: compound, comminuted fracture of the left orbital region of the skull, severe

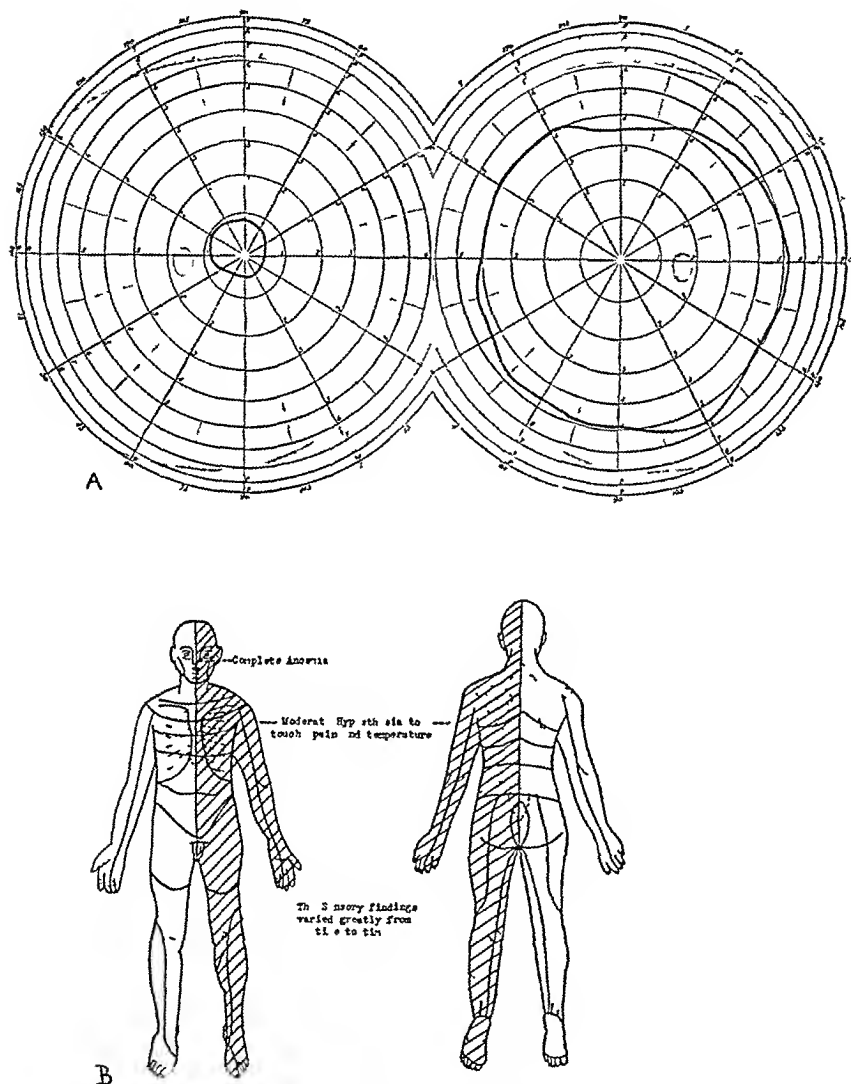


Fig 33 (case 24)—*A*, Tubular vision in the left eye (The representation of the visual field was transferred from the universal perimeter). Corrected vision was 20/200—in the left and 20/70—in the right eye. *B*, moderate hysterical sensory disturbance present thirteen months after a head injury. Marked improvement occurred nine years later.

concussion and contusion of the brain, primary atrophy of the left optic nerve of moderate degree, changes in the choroid, mental deterioration, manifestations of hysteria superimposed on the organic picture.

deep reflexes were normal except the right knee jerk, which seemed quicker than the left. No abnormal reflexes of the Babinski type were noted. The blood pressure was 220 systolic and 120 diastolic.

Roentgenograms of the skull showed a suspicious small linear fracture in the right sphenoid region, crossing the sella.

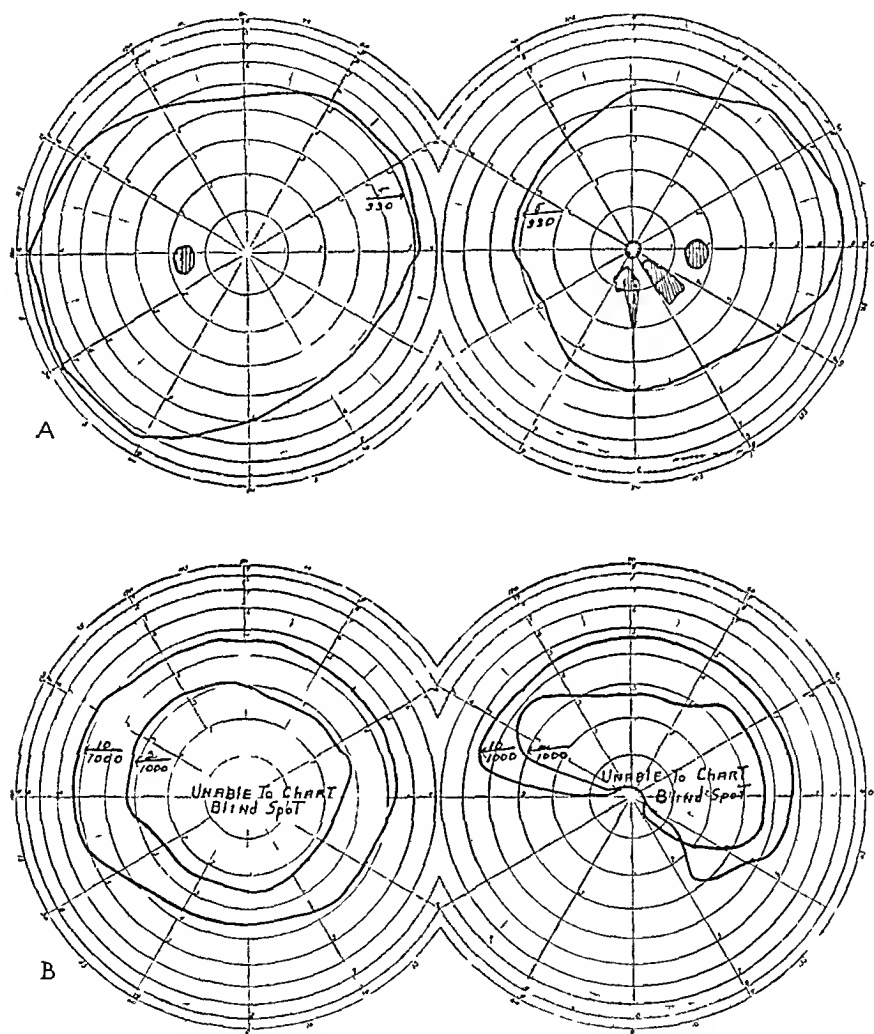


Fig 29 (case 21)—*A* fields showing central and paracentral scotomas on the right three months after a head injury (The representation of the right field was transferred from McHardy perimeter) *B*, fields showing peculiar contraction on the right five and a half months after injury. Hysterical hemianesthesia appeared at about this time. At the first examination vision in both eyes was reduced to counting fingers only, at the second examination uncorrected vision was 20/30 in the left and 20/200 in the right eye.

*Impression*—The following conditions were considered to be present: concussion and contusion of the brain, probable fracture of the skull. The sudden

# INTERACTION OF BONE AND VARIOUS METALS

VANADIUM STEEL AND RUSTLESS STEELS

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The interactions that occur between bone and metal are exceedingly complex. Almost without exception, past experiments have been limited to observation of the changes that occur in bone when the metallic foreign body is inserted in it. The problem cannot be solved from this point of view alone. The question does not involve merely the reaction of bone to metal but is concerned as much with the changes that occur in the metal when it is buried in bone.

A basic consideration is that the exact chemical composition of the metal tested must be known. Although this seems obvious, the omission of data on the composition of the metal from previous studies probably accounts for variations in the results. Only a few metals are relatively pure, the majority containing other substances in varying amounts, and alloys, or metal mixtures, which seem closely related may be chemically dissimilar. The inclusion of data on the composition of the metal used in future experiments will go far toward insuring comparable statistics.

We recommend that the following postulates be adopted for studies of this nature: (1) The exact chemical composition of the metal used should be known rather than the generic name. (2) The reaction of the metal to bone should be studied as well as the reaction of bone to the metal.

Four alloys were chosen for investigation, one of vanadium steel and three of rustless steels of different composition. It will be necessary to explain briefly the reasons for the choice of these specific alloys. In December 1930 the American College of Surgeons requested the assistance of the United States Bureau of Standards in the establishment of a standard Lane plate. This committee met in November 1930, with Dr. Phillip D. Wilson acting as chairman. The other members consisted of several physicians interested in the subject and representatives of several manufacturers of these appliances. As the result of their deliberations a set of standards was adopted for the numerous Lane

From the Orthopedic and Surgical Services of the Menorah Hospital

(fig 31) The patient also complained of blurring of vision in the left eye. Perimetric determination of the fields made on Nov 26 1934, showed a beginning contraction of the left field (fig 31). The patient subsequently returned to lighter work and the manifestations of hysteria cleared up.

*Impression*—Concussion of the brain was thought to be present. The manifestations of hysteria developed nine months after the injury when the patient was physically unable to do heavy work.

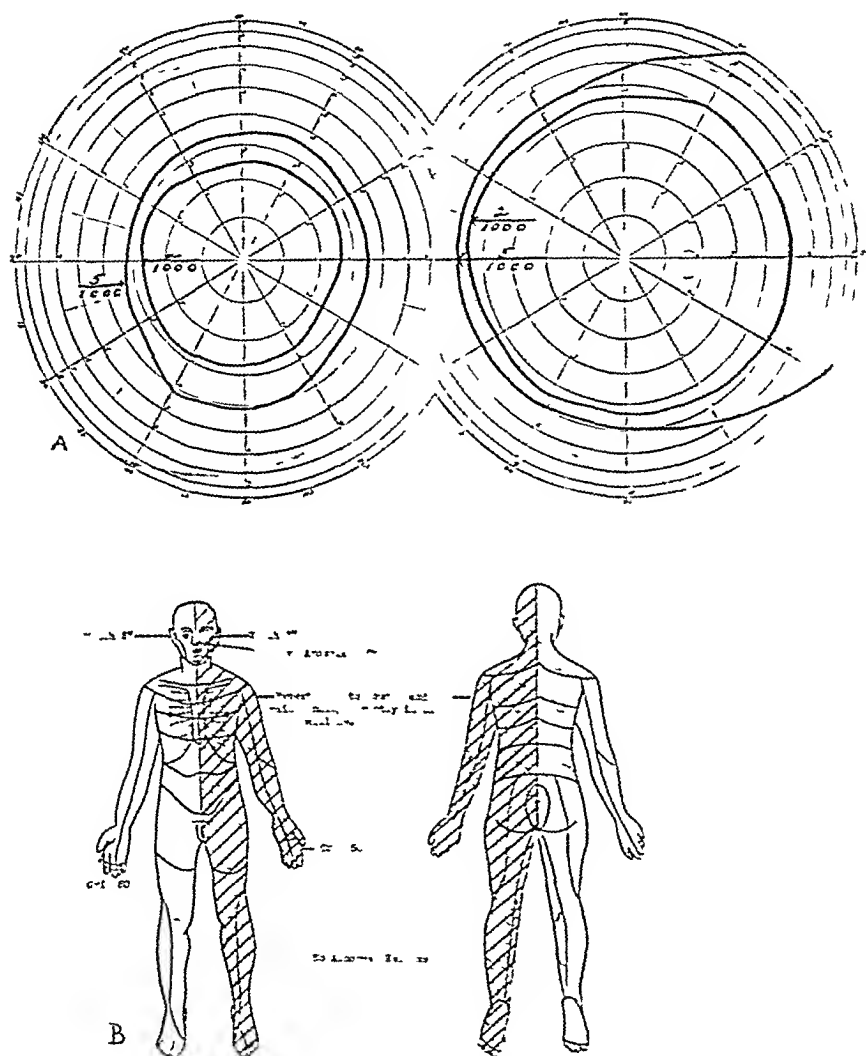


Fig 31 (case 22)—*A* moderate contraction of the left visual field probably functional. Uncorrected vision was  $20/30 \pm \pm$  in the left and  $20/50 \pm \pm$  in the right eye. *B* sensory changes due to moderate hysteria coincidental with alteration in the ipsilateral field. Both appeared when the patient began to do heavy labor and cleared up when his occupation was changed.

*CASE 23*—Marked contraction of the right visual field (probably hysterical) appearing approximately three days after a minor head injury.

J. C., a man aged 46, married, a laborer, was referred by the Union Oil Company on Nov 10 1931. The injury occurred on Oct 12 1931 when the patient



tungsten. The balance of the ingredients are iron, carbon and impurities."<sup>4</sup> In Zierold's work the terms "stellite" and "rustless steel" were used interchangeably. Inspection of the formula renders the term "rustless steel" for an alloy of this composition extremely questionable.

At the present time significant work is being done on this subject by Menegaux, Moyses and Odiette. They have found that there is no inhibition of growth in cultures of osteoblasts and fibroblasts when small disks of chrome-nickel steel alloys are added to them.<sup>5</sup> At the same time they found that gold, aluminum and lead have similar biologic action but cannot be recommended for osteosynthesis for physical reasons. The metals which they found to be nontoxic when tested by this method have the following European trade names: Duralumin, V<sub>2</sub>A extra, Nicral D and Platino-stainless D. The formula for Duralumin is: copper, 4 per cent, magnesium, 0.5 per cent, manganese 0.2 per cent and silicon from 0.3 to 0.5 per cent, the remainder consisting of aluminum. V<sub>2</sub>A extra is made up as follows: chromium, 18 per cent, and nickel, 8 per cent, plus a small unspecified percentage of manganese and titanium. The formula for Nicral D is: chromium, 20 per cent, and nickel, 16 per cent. The formula for Platino-stainless D is: chromium, 18 per cent, and nickel 8 per cent, plus a small unspecified amount of tungsten. To quote directly, they "inhibit neither growth nor migration of osteoblasts or fibroblasts in vitro."

A large number of appliances for the internal fixation of bone made of rustless steel have been designed. The most outstanding example, of course, is the Smith-Petersen nail, but there are many others, including Steinmann pins and bone screws of special design.<sup>6</sup>

The term rustless steel requires definition. We did not know and we believe that the members of the medical profession generally do not recognize that the adjective "rustless" or "stainless" is applied to many alloys of dissimilar composition. They have this in common. They are all alloys containing from 7 per cent to much higher percentages of chromium and are low in carbon content. Nickel may be absent or may be present in a large quantity. In the presence of the higher percentages of nickel the amount of chromium is decreased.

4. Haynes "Stellite" Company. Personal communication to the authors.

5. Menegaux, G., Moyses, P., and Odiette, D. Croissance des tissus conjonctifs et osseux cultivés "in vitro" en présence de certains métaux, *Presse med* **42**: 658 (April 21) 1934.

6. Smith-Petersen, M. N., Cave, E. F., and Vangorder, G. W. Intracapsular Fractures of the Neck of the Femur, *Arch Surg* **23**: 716 (Nov.) 1931. Jones, Laurence. Intracapsular Fractures of the Neck of the Femur, *Ann Surg* **97**: 237 (Feb.) 1933. Henry, Myron O. Intracapsular Fractures of Hip. New Device for Lateral Osteosynthesis, *J Bone & Joint Surg* **16**: 168 (Jan.) 1934.

traumatic, and it was believed that the changes in the left optic nerve would be slowly progressive. This proved to be the case.

There were marked alterations in the form fields. On August 27, 1924, there was a typical hysterical contraction of the left field (fig 33), on Nov. 13, 1925, this field had widened, and on June 17, 1926, it had again contracted.

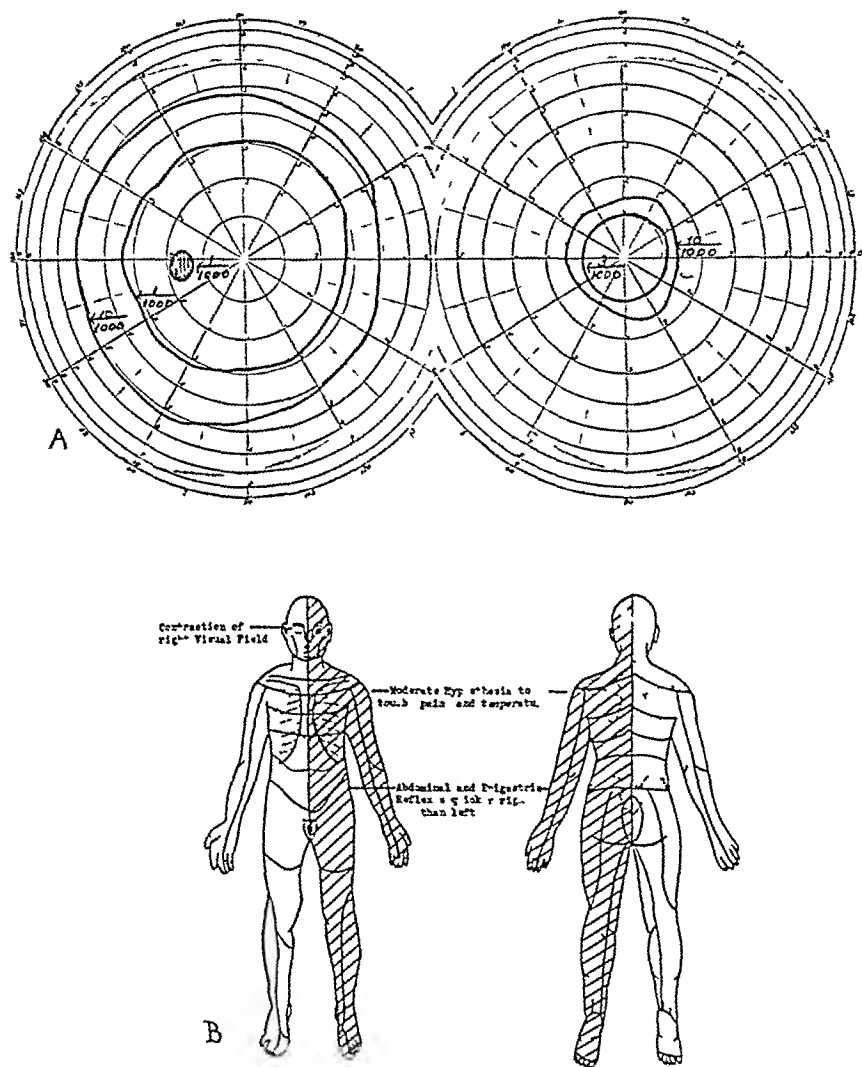


Fig 32 (case 23)—*A*, hysterical contraction of the right visual field, present approximately nineteen months after head injury. In the left eye uncorrected vision was 20/40+, with the right eye the patient saw the card only. *B*, hysterical sensory changes coincidental with the contraction of the field. Both of these conditions improved when the patient was given a different occupation.

During the entire period of observation the pupils remained equal and reacted quickly to light and in accommodation. The extra-ocular movements were normal in all respects. On Aug 28, 1924, complete bilateral anosmia was discovered. At times hypæsthesia to touch, pain and temperature was described on the left side.

## SUMMARY AND CONCLUSIONS

A brief resume of the literature concerning traumatic lesions of the visual pathways is presented. Twenty-four cases in which various types of alterations in the fields followed craniocebral injuries are reported.

An anteroposterior splitting of the chiasm apparently may result from a blow directed to the top of the head. Under such circumstances a contre-coup effect on the chiasm is brought about, even though the exact mechanism of its production is not clear.

plates of the Sherman type<sup>1</sup> They were to be made of a vanadium steel alloy known as Society of Automotive Engineers steel 6150, having the following composition

Substance	Percentage
Carbon	0.45-0.550
Manganese	0.50-0.800
Chromium	0.80-1.100
Phosphorus	not over 0.040
Sulfur	0.045
Vanadium	{ not under 0.150 desired 0.180

This alloy was recommended to Dr. Sherman by the engineers of the Carnegie Steel Company in Pittsburgh because it has great surface hardness. No physiologic tests were made.<sup>2</sup> It was thought that this would end two outstanding faults, the breakage of plates and the loosening of screws. Such has not been the case, and the reasons will be shown later.

Before 1924 rustless steel was not generally employed in bone surgery, but the work of Zierold gave an immediate stimulus to its extensive use.<sup>3</sup> A study was made of the reaction of bone to gold, silver, aluminum, zinc, lead, copper, nickel, high carbon steel and low carbon steel, stellite, copper-aluminum alloy, magnesium and iron. A finding of Zierold's and one which has not been given the recognition it deserves was that low carbon steels and high carbon steels produced extensive bone necrosis and were in fact, the most irritant of any of the substances tested. This point is deserving of emphasis as one still sees competent surgeons inserting carpenter's screws and nails in bone. Zierold's final conclusions were that aluminum, gold and stellite 'tend to become encapsulated with but little hindrance to the reparative process. They are inert materials unaffected by the living cells and body cells.' In reference to the reaction of bone to stellite he concluded that it showed "the least departure from the normal. The type of reaction is similar and the degree is not outside the limits observed in the controls. In fact, it appears the metal merely occupies space affecting in no way the regeneration of bone and periosteum."

Recently the formula for this stellite was obtained. This is, approximately "58 per cent cobalt, 35 per cent chromium and 4 per cent

1 Steel Bone Plates and Screws, United States Dept. Commerce Bureau of Standards Commercial Standard CS37-31

2 Wilson, Phillip D. Personal communication to the authors

3 Zierold, A. A. Reaction of Bone to Various Metals, Arch. Surg. 9:365 (Sept.) 1924